THE American Journal OF Gastroenterology

VOL. 25, NO. 6 JUNE, 1956

1955 AMES AWARD LECTURE:
Disorders of the Digestive System

Adrenal Influences Upon the Gastrointestinal Tract

Phrenic Nerves and Gastrointestinal Mechanisms

Newer Trends in Caudal Anesthesia

Gluten Sensitivity—Sprue?

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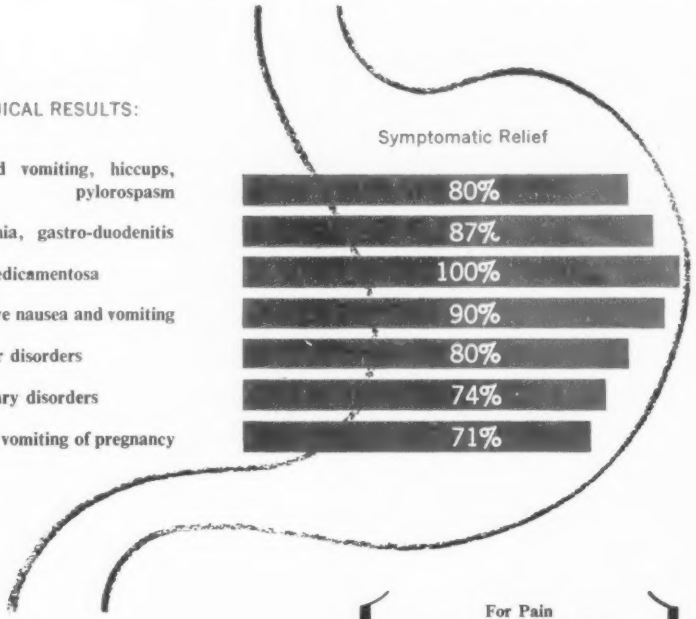

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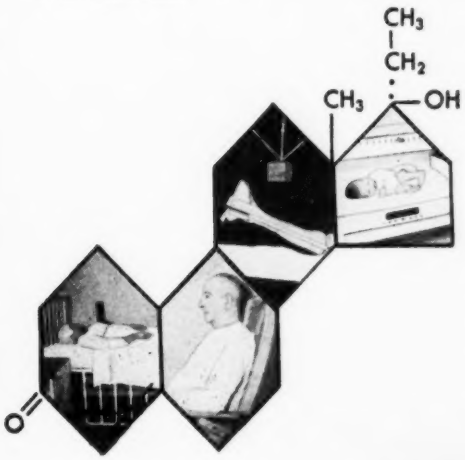

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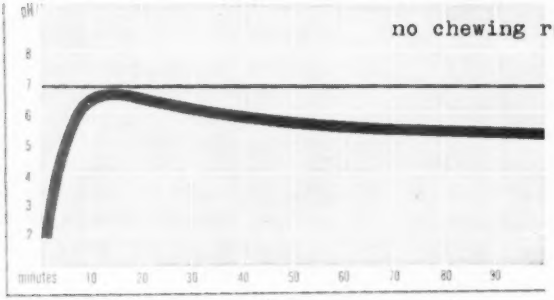

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THE American Journal OF Gastroenterology

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The Pioneer Journal of Gastroenterology, Proctology and Allied Subjects in the United States and Canada

contents:

Editorial Board and General Information 518

1955 AMES AWARD LECTURE:

Disorders of the Digestive System: Brief Review of Major Existing Problems ..... GEORGE B. EUSTERMAN, M.D., F.A.C.G. (Hon.) 525

Adrenal Influences Upon the Gastrointestinal Tract ... SEYMOUR J. GRAY, M.D., Ph.D., COLIN G. RAMSEY, M.D., ROBERT W. REIFENSTEIN, M.D. and LEWIS J. KRAKAUER, M.D. 532

Phrenic Nerves and Gastrointestinal Mechanisms. Left Phrenic Crush and Vagotomy ..... N. C. JEFFERSON, M.D., U. G. DAILEY, M.D., L. WALKER and H. NECHELES, M.D., Ph.D., F.A.C.G. 545

Two Cases of Carcinoma of the Stomach Surviving After Surgery More Than Twelve and Eight Years Respectively ..... JAMES TESLER, M.D., F.A.C.P., F.A.C.G. and MICHAEL SCIMECA, M.D., F.A.C.G. 550

Newer Trends in Caudal Anesthesia ..... MAX S. SADOVE, M.D., MYRON J. LEVIN, M.D., RAYMOND F. ROSE, M.D. and FRANCIS A. TORREY, M.D. 555

Gluten Sensitivity—Sprue? ..... JOSEPH LITWINS, M.D., F.A.C.P. 562

Carcinoma of the Descending Colon to the Rectosigmoid PETER A. ROSI, M.D. 571

X-ray Lesions of the Small Bowel ..... L. K. BEASLEY, M.D. 575

Colonic Diverticulitis .... THEODORE S. HEINEKEN, M.D., F.A.C.P., F.A.C.G. 584

Carcinoma of the Sigmoid Colon Discovered During Examination for Acute Intussusception of the Sigmoid .... HARRY A. FEIGENBAUM, B.S., M.D. 591

President's Message 593

News Notes 594

Abstracts for Gastroenterologists 595

Book Reviews for Gastroenterologists 610

Index to Volume 25 611

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Index to Advertisers

Ames Co., Inc. 524
Borden Co., The 624
Burton, Parsons & Co. ..... 3rd cover
Ciba Pharmaceutical Products, Inc. 623
Desitin Chemical Co. 520
Hoffmann La Roche, Inc. 516
Lakeside Laboratories, Inc. 522
Pfizer Laboratories 523, 621
Photovolt Corp. 622
Rorer, William H., Inc. ..... 2nd cover
Schering Corp. 521
Searle, G. D., & Co. 515
Sharp & Dohme 622
Upjohn Co., The 619
Warner-Chilcott Laboratories ..... 4th cover
Winthrop Laboratories, Inc. 626
Wyeth, Inc. 519, 625

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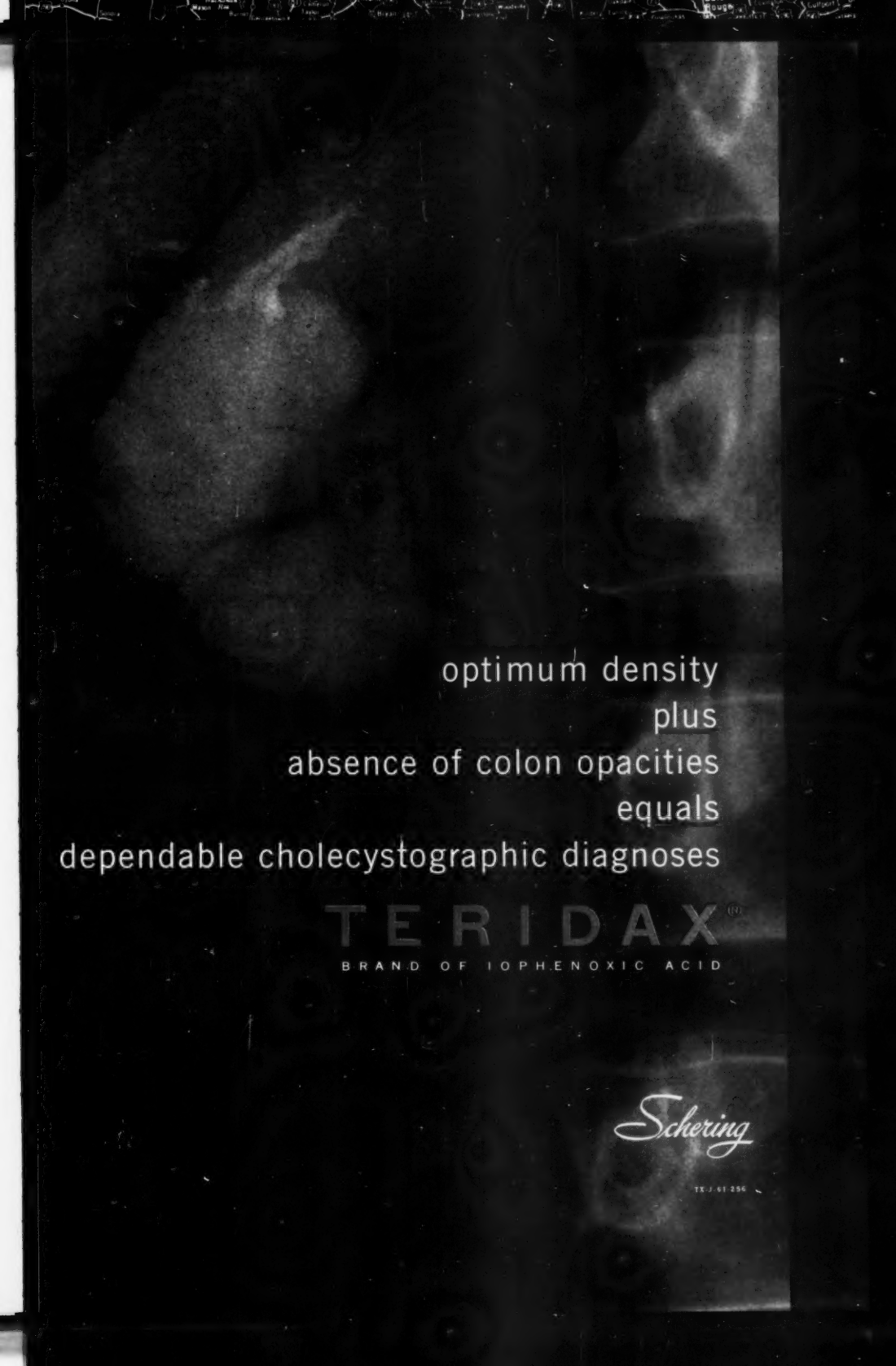
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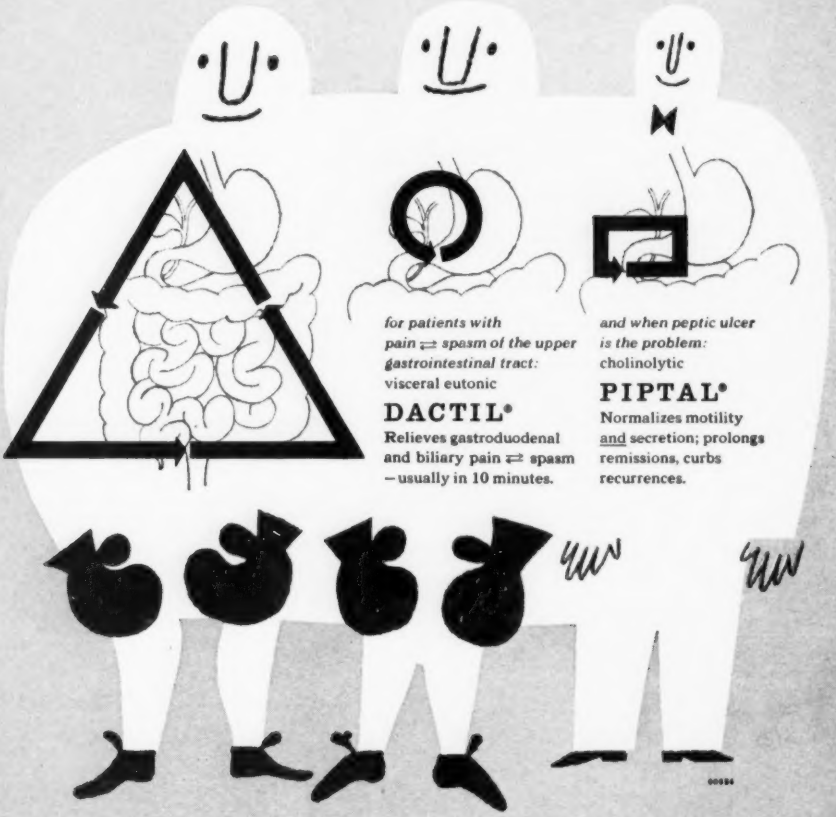

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1955 AMES AWARD LECTURE

DISORDERS OF THE DIGESTIVE SYSTEM: BRIEF REVIEW OF MAJOR EXISTING PROBLEMS*

GEORGE B. EUSTERMAN, M.D., F.A.C.G. (Hon.)†

Rochester, Minn.

I feel greatly honored in having been invited by your College to give the first Ames Award Lecture. It also seems fitting that on this occasion all of us do honor to those distinguished past and present members of this city's profession who have made invaluable contributions to our chosen field of medicine.

An advance copy of the abstract of papers to be presented at this convention reflects an extensive and diversified scientific program. While it is unavoidable that I will also deal with some of the topics to be presented, my observations will be more in the way of generalizations perhaps, while those of my fellow participants, dealing almost exclusively with single entities, will be more specific and detailed.

The unprecedented medical progress of the last half century has greatly increased our knowledge of the functions of the human organism in health and disease. The vast, almost bewildering accumulation of literature during this period dealing with dysfunction and diseases of the entire digestive system attests to the abiding interest of a large portion of the profession in this field. We are witness to an era of so-called miracle drugs, to indispensable objective visualizing methods of diagnosis, to great advances in biochemistry, anesthesia, investigative and surgical technics and complex instruments of precision. In the last few decades more active and fruitful research than heretofore has been directed to disorders of the esophagus, biliary tract and pancreas.

*Presented before the Second Annual Convention of the American College of Gastroenterology, Chicago, Ill., 24, 25, 26 October 1955.

†Emeritus Member, Section of Medicine, Mayo Clinic and Mayo Foundation.

The Mayo Foundation, Rochester, Minnesota, is a part of the Graduate School of the University of Minnesota.

Notwithstanding such unparalleled progress, problems bearing on pathogenesis, diagnosis and therapy persist. Inasmuch as some of these are fundamental, their solution constitutes a formidable challenge.

The Upper Digestive Tract

Lack of precise knowledge concerning the factor or factors which initiate a disease process defeats efforts at prevention and makes treatment largely empirical. What do we actually know about the etiology of cholecystic disease, pancreatitis, regional enteritis, ulcerative colitis, of gastric and duodenal ulcer, or of their congeners, erosive and ulcerative gastritis, for that matter? The ultimate solution of these and allied problems apparently awaits plodding, unspectacular research in the basic sciences.

The problem of pathogenesis is well illustrated by that ubiquitous wound stripe of civilization, chronic benign peptic ulcer. Despite an enormous amount of research directed to its solution throughout the years, definitive conclusions have not been reached. Of the various theories of ulcer causation entertained in the past, the neurogenic and chemicomechanical have best stood the test of time. In the main the role of emotional and physical stress on nervous, hormonal and humoral functions giving rise to pathophysiologic processes in the upper digestive tract dominates current thinking. The baneful effect of emotional stress on human gastric and intestinal mucosa which characterizes the alarm-reaction phase of the general adaptation syndrome of Selye seems to be amply confirmed. The convictions of our European colleagues are not dissimilar. Leading authorities, briefly stated, look on chronic ulcer as a disease of the vegetative nervous system chiefly affecting the hypothalamic component of the parasympathetics, resulting in an unchecked anarchic activity of the hypothalamic centers. All the foregoing observations especially apply to duodenal ulcer. The corrosive and digestive action of the gastric juice undoubtedly plays an all-important role, certainly in chronicity of the lesion.

But a highly probable inciting factor, apart from acid-pepsin, and heredity demand consideration. As regards the former, it is not unreasonable to presume that it could be a toxic metabolite. For example, Eyring and Daugherty have advanced the intriguing theory that stress sets off a destructive chain reaction among the body cells, with histamine or histamine-like substances acting as the destructive agent.

The heretofore rather nebulous role of constitution and heredity in the formation of ulcer has been clarified considerably by the controlled convincing study in heredity, physique, and personality of the Swedish investigator, Wretmark. His observations justified the conclusion that an inherited predisposition to duodenal ulcer exists and that superstability is an essential factor in this predisposition. Moreover, the study had an important prognostic bearing. About two-thirds of the patients with duodenal ulcer could be divided into two widely

different prognostic groups. The course of the disease was favorable in 44 per cent of the patients who were substable and of wide-heavy body build; it was favorable in only 9 per cent of the group of superstables of tall-narrow body build. This type of investigation apparently did not lend itself to clarification of the role that heredity plays in gastric ulcer.

Hypersecretion of gastric juice, predominantly of nervous origin, is present in the majority of patients with duodenal ulcer. To the increased corrosive properties of this secretion is attributed the formation of duodenal ulcer by Dragstedt and others. In this connection, several English investigators reported that there were 75 per cent more parietal cells in males with duodenal ulcer than in nonulcer males. The maximal secretory capacity of the ulcer group was 72 per cent higher than that of the nonulcer one. Thus anatomic structure appears to be linked up with function, and this fact should throw further light on the ulcer problem.

What about the formation of gastric ulcer in relation to the increased corrosive action of the gastric juice? Dragstedt contends that the same chemical factor is at work. He attributes the hypersecretion of gastric juice in such patients to hormonal origin, the result of hyperfunction of the gastric antrum in the presence of food in the stomach, and states that the hypersecretion is abolished by excision of the antrum. On the basis of clinical observations, his conclusions in this respect cannot be unreservedly accepted. In the majority of patients with gastric ulcer, gastric chemism is characterized by normal to subnormal volume and acid-pepsin concentration as well as hypomotility. That chemical corrosion is the sole causative factor in the initial phase of spontaneous ulcer in the intact human stomach is still disputed. For example, a duodenal ulcer may go into complete remission, and heal spontaneously or following treatment, even though the secretory milieu which characterizes such ulcer persists or promptly returns to the original status following treatment. It has also been observed that college students with persistent though symptomless hypersecretion may eventually develop an acid dyspepsia but not an ulcer. The presence of free hydrochloric acid, however, appears to be essential to ulcer formation, at least to its chronicity, even in minimal concentration, and undoubtedly plays a predominant if not exclusive role in the formation of jejunal ulcer.

On the other hand, the French investigators, Frumusan and Cattan, stress the psychosomatic factor as embodied in their corticovisceral hypothesis. They regard gastroduodenal ulcer as a gastric manifestation of generalized illness and state that ulcer results from a disturbance of corticogastric dynamics, producing hypersecretion, muscular spasm and spastic vascular occlusion. The role of the corrosive action of the gastric juice is not considered of primary importance. These disturbances may be the result of external factors, such as emotions and conflicts, or internal factors, such as gastritis, appendicitis,

cholecystitis, or colitis. They contend that ulcer results from autodigestion of an ischemic area on a vascular basis. As proof of this theory, they injected procaine into the white matter of the frontal lobe, a procedure which interrupts the pathways between the anterior and dorsimedial nuclei of the hypothalamus and prefrontal gray matter. This resulted in prompt cessation of pain and healing of the ulcer in three severe cases. As previously stated, the emotogenic factor and its bearing on autonomic activity dominates the thinking of most authorities at home and abroad. There is disagreement as to the predominant or primary role that the chemical and vascular factors respectively play. Progress is being made, however, and it is to be hoped that the solution of this baffling problem will soon be at hand.

Of course the $64,000 problem is the earlier recognition of gastric cancer. I shall, however, limit my consideration to one aspect of it, namely the differentiation of benign and carcinomatous ulcer. The profession is alerted to the fact that about 15 per cent of gastric carcinomas masquerade as benign ulcer. The niche-like lesion projecting beyond the luminal outline of the stomach is especially deceptive. Conventional diagnostic measures will not disclose any definitive malignant characteristics unless the defect is intraluminal. Careful consideration of all available symptoms and signs and of the degree of response to adequate medical management in hospitals, objectively as well as subjectively, especially the former, is essential. Recently, several authorities have stated that failure of successful differential diagnosis by competent specialists should not exceed 6 per cent. To further enhance diagnostic accuracy one can even resort to biopsy and cytologic examinations whenever necessary and available. According to Rubin and his associates 109 of 111 proved gastric lesions, 42 of which were malignant, were correctly diagnosed, when all diagnostic methods were used. Thus, under ideal circumstances diagnosis of the nature of gastric lesions is almost becoming an exact science. While the evidence afforded by the response to adequate treatment in hospitals is highly important, one must remember that occasionally a carcinomatous ulcer to all intents and purposes has completely healed following treatment. The implications are obvious, namely periodic re-examination of all nonsurgically treated patients, especially those 40 years of age and older. (Here the author presented slides and tables illustrating differential diagnostic aspects of benign and carcinomatous gastric ulcers.)

With respect to hemorrhage, *conventional* clinical and laboratory procedures often furnish no timely trustworthy information as to whether or not such hemorrhage will prove fatal in the individual case. Kruger and his associates, however, have shown that reliable quantitative tests are now available by using human serum tagged with I^{131} according to the method of Crispell and associates. With a single initial blood volume determination extent of hemorrhage can be objectively measured and specific requirements for whole blood plasma or washed red cells estimated. As Tabern will show the

easiest and most reliable method of quantitating gastrointestinal bleeding (blood and red cell volume) is that of tagging the red cells with Rachromate (Cr^{51}). Such determinations can readily be repeated as necessary. The risk of pulmonary edema and other baneful effects resulting from massive transfusions is avoided. In institutions in which such measures are routine, the mortality has been gratifyingly reduced, especially in the most severe categories. In this connection I would like to re-emphasize the fact that quantitative determinations which, apart from radioactive isotopes, reliably mirror functional derangement in diseased organs, like the kidneys for example, are as yet infrequent in diseases of the organs of digestion, although the liver is now proving to be an exception.

The Biliary Tract and Pancreas

Problems concerned with the diagnosis, treatment and pathophysiology of disorders following cholecystectomy, like that following gastric resection, continue to plague us. In the case of the former, diagnosis and therapeutic indications are expedited if the operation was competently performed for bona fide disease. Former difficulties have been minimized somewhat by accretions to our knowledge as to the morbid processes which can give rise to unsatisfactory outcome such as inflammation or stone or both in the stump of the cystic duct, fibrous stricture of the terminal portion of the common duct, and hepatic duct stones, which occur in an average of 7.4 per cent of all patients with cholelithiasis; by resort to such diagnostic maneuvers as transduodenal biliary lavage, to preoperative and postoperative cholangiography, being, however, mindful of their limitations. In less competent hands one must also reckon with erroneous diagnosis, with injury to vital structures, stricture, residual duct stones and extensive adhesions interfering with function of neighboring viscera.

While tests of liver function and liver biopsy have contributed greatly to diagnosis and to our understanding and evaluation of changes during the course of parenchymatous disease, the pathologic process underlying jaundice for example, is still more readily recognized by clinical methods. A major diagnostic problem is the failure of such tests to differentiate cholestasis of intrahepatic origin from cholestasis of extrahepatic origin. Both of these conditions give the same laboratory results; yet the treatment of the former is medical, and the treatment of the latter is surgical.

The diagnosis of pancreatic carcinoma and chronic relapsing pancreatitis, especially in their earlier stages, is beset with more difficulties than that of any other organ of the digestive system, for reasons with which all of us are familiar. Recognition of pancreatic carcinoma in the absence of jaundice, or involvement limited to the terminal portion of the gland, poses a real problem. Moreover, roentgenologic defects of the stomach, especially in nonicteric cases,

may make pancreatic carcinoma indistinguishable from gastric carcinoma. The diagnosis of fairly advanced cases of chronic pancreatitis can usually be made by a process of exclusion and time-honored roentgenologic and laboratory methods. Unfortunately, the secretin test in the opinion of many colleagues, as a routine diagnostic measure, even in well-equipped hospitals and clinics, is impracticable because it is time-consuming, is beset with technical and interpretative difficulties, is expensive, and unfavorable reactions to the stimulus are not uncommon. One must be dedicated to the task like Dreiling. Numerous attempts to devise simpler tests of pancreatic function, thus far not dependable, are proof of this.

Therapy

Solution of the problem of successful medical treatment of chronic inflammatory and ulcerative lesions of the stomach and intestines still eludes us. Undoubtedly, this is due in large measure to lack of definitive knowledge of pathogenesis. The approved conventional method and ancillary measures of treatment for gastric and duodenal ulcer, when meticulously planned and carried out, permit of healing in a high percentage of uncomplicated cases which have not reached too chronic a stage. It is not so much the problem of healing the lesion as of keeping it healed, that is, of preventing recurrences. Authoritative follow-up studies 5 to 10 years after one or more courses of treatment reveal a discouragingly low number of "cures", ranging from 15 to 50 per cent, with an average of about 30 per cent. Personal experience and repeated observation, however, have convinced me that it is not so much the method of treatment that is at fault as that it has frequently not been adequately applied, coupled with lack of the patient's cooperation, which must be cultivated from the outset. In numerous instances there is considerable justification for the saying, "It is the patient, not the ulcer, that is incurable."

We are all mindful of the great difficulty of adequate neutralization of the acid gastric contents throughout the 24-hour period by routine measures. Hence the present-day attempts at interference with the formation of hydrochloric acid within the parietal cells by carbonic anhydrase inhibitors such as Diamox. This is promise of a step in the right direction, but it remains to be seen whether such measures can be applied successfully in the ulcer patient.

The treatment of chronic ulcerative colitis also presents many problems, and in the main the results have not been too encouraging. In the hands of those who have highly specialized skill and who carry out treatment of favorable cases in thorough fashion over adequate periods of time, however, many patients pursue gainful occupations and are spared surgical intervention.

Apart from carcinoma, regional enteritis is the gravest of intestinal lesions. In contradistinction to ulcerative colitis, even radical surgical treatment cannot be relied on to cure the disease. In a recent review of 610 cases by several of

my colleagues, 400 of the patients were submitted to operation. Briefly stated, in only one out of three was the disease arrested for an average of 2 years.

And now I come to the close of a somewhat sketchy discussion. Since much of the subject matter is controversial, I do not expect you to share my convictions in all respects. In due time, many of these and other problems will be resolved. This presupposes, however, increased research in the basic and applied sciences, the pressing need of which has been emphasized recently by leading clinicians and investigators in our chosen field. As a matter of fact, we have not kept pace in this respect with other disciplines. There are those among you who have been earnest and fruitful investigators, who will continue to be so and will inspire fellow members so inclined to do likewise.

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ADRENAL INFLUENCES UPON THE GASTROINTESTINAL TRACT*

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Studies previously reported from this laboratory have indicated that the administration of ACTH and cortisone over a period of days or weeks induces a significant increase in the basal and nocturnal gastric secretion of acid and pepsin, with a similar concomitant increase in uropepsin excretion to levels commonly observed in patients with active peptic ulcer. This has been confirmed by a number of investigators[1-6]. The development of epigastric pain, acute or chronic duodenal ulcer *de novo,* or the reactivation of quiescent ulcer disease with subsequent hemorrhage or perforation, following the administration of these hormones, is invariably accompanied by a considerable increase in uropepsin excretion. It has been postulated, therefore, that the stomach acts under adrenal control through a hypothalamic-pituitary-adrenal-gastric pathway[7]. To further clarify this relationship, the uropepsin excretion was determined in patients with adrenal and pituitary insufficiency, before and after hormone replacement therapy, and in patients with adrenal and pituitary hyperactivity.

Method

The uropepsin excretion was determined in the following groups of individuals: 265 normal subjects and patients without demonstrable gastrointestinal disease; 205 patients with active and inactive duodenal ulcer; 90 patients with gastric ulcer; 60 patients with gastric cancer; 26 patients who had undergone subtotal gastric resection; 10 patients following total gastrectomy; 26 patients following vagectomy and 70 patients with pernicious anemia. The response to hormone stimulation was measured in 80 subjects and the uropepsin excretion was evaluated in the following endocrine states: Addison's disease, hypopituitarism, Cushing's disease, adrenogenital syndrome, myxedema and hyperthy-

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roidism. In all cases three or more 24-hour specimens, collected under controlled conditions, were analyzed to establish the mean output of a given individual.

The 24-hour urinary excretion of uropepsin was determined by our modification of the methods described by Bucher and Anson and Mirsky as reported previously[8,9,10].

Twenty-four-hour urine specimens were collected using 2 to 5 c.c. of 50 per cent sulphuric acid or toluene as a preservative and refrigerated immediately. The volume of urine was measured and recorded along with the time of the collection period. (Determinations may be performed on specimens collected over less than a 24-hour period provided the exact time of collection is known. In such instances a 12-hour urine has been found to be the most satisfactory substitute for a 24-hour urine collection).

The pH of a 20 c.c. aliquot of urine was determined using a Beckman glass electrode pH meter. The urine aliquot was then acidified, using 1.15 N HCl, until the final pH was 1.5. (If more than 5 c.c. of 1.15 N HCl was required, the sample should be discarded and another 20 c.c. aliquot taken and acidified with 3.5 N HCl). The acidified aliquot was then made up to a volume of 25 c.c. with distilled or demineralized water. One c.c. of this acidified urine was incubated with 5 c.c. of 2.5 per cent denatured acidified hemoglobin substrate at 37°C for 30 minutes. (The substrate* is acidified on the day of the analysis by the addition of enough 0.3 N HCl to make a final pH of 1.5). Ten c.c. of trichloracetic acid were added to stop the reaction. The specimen was then filtered and the concentration of tyrosine-like substances in 5 c.c. of the filtrate was determined by the Folin-Ciocalteau procedure[11] with the use of a photoelectric colorimeter, using a green filter with a spectral range of 500-570 mu.

To correct for chromogenic substances present in the urine and substrate, prior to proteolysis, 1 c.c. of the acidified diluted urine and 5 c.c. of hemoglobin substrate were added directly to the trichloracetic acid and filtration was carried out. The filtrate was then treated and analyzed in exactly the same manner as described above.

The difference in the colorimeter readings between the incubated and unincubated specimens indicated the degree of production of tyrosine-like substances resulting from proteolysis. Peptic units were then calculated with the aid of a standard curve.

The standard tyrosine curve relating the colorimeter readings to known amounts of tyrosine in 5 c.c. of filtrate must be constructed. To do this, solutions of gradually increasing concentrations of tyrosine dissolved in 0.2 N HCl are made up, (i.e., 0.016, 0.032, etc. to 0.64 mg. per c.c.). One c.c. of each of these

*The substrate powder may be obtained commercially from the Wilson or Armour Companies.

solutions is then incubated with 5 c.c. of 2.5 per cent acidified hemoglobin substrate at 37°C for 30 minutes using as a blank an unincubated mixture of 1 c.c. of 0.2 N HCl and 5 c.c. of 2.5 per cent hemoglobin. Thereafter the same procedure as outlined above for uropepsin is followed. The difference in colorimeter readings obtained by subtracting the reading of the 5 c.c. of filtrate of the unincubated control specimen from the reading for the incubated specimen therefore represents the color value of known concentrations of tyrosine minus any color derived from the acidified hemoglobin substrate. When these differences are plotted on a graph against the known concentrations of tyrosine per 5 c.c of filtrate, a straight line relating colorimeter differences to tyrosine concentrations is obtained. Utilizing this standard curve, any colorimeter differ-

TABLE I

STRESS FACTORS IN UROPEPSIN EXCRETION

	Number of Patients	Uropepsin Excretion (units/24 hrs.) Mean
Normal	265	3,670
ACTH and Cortisone	80	12,536
Physical Stress		
Acute	25	22,000*
Chronic	20	10,000*
Active Duodenal and Gastric Ulcer	295	7,642
Vagotomy		
Basal Conditions	13	6,500
ACTH or Stress	6	24,000*
Resection of Gastric Antrum		
ACTH or Stress	12	26,000*

*Denotes maximum response.

ence obtained for unknown urine plus hemoglobin substrate can be directly converted to mg. of tyrosine per 5 c.c. of filtrate.

The unit of activity of uropepsin was defined in this study as that amount which during 30 minutes of incubation at 37°C in the standard assay released 0.04 mg. of tyrosine-like substances. Results were expressed as units per c.c. of undiluted urine or units excreted in 24 hours. To convert mg. of tyrosine to peptic units therefore simply *divide* the amount of tyrosine released by 0.04 mg. Multiplying this value, which represents the concentration per c.c., by the total volume of urine excreted in 24 hours gives the number of units excreted in a 24-hour period.

Results

Normal Uropepsin Excretion:—The uropepsin excretion of 265 normal subjects and patients without demonstrable gastrointestinal disease, varying in age from 15 to 83 years, ranged from 1,000 to 6,000 units, with a mean output of 3,670 units in 24 hours and a standard error of ± 159 units (Table I). There did not appear to be any significant difference between men and women, nor did age alter the uropepsin levels, except in the group over 70 years. The mean excretion of 15 patients in the 70 to 83 age group approximated 1,779 units.

The uropepsin excretion appeared constant for each individual in spite of wide variations in the urine volume, and remained relatively constant during various periods throughout the day. Daily fluctuations in dietary intake did not alter the uropepsin level significantly.

Effect of Adrenal Steroids upon Uropepsin Excretion:—The increase in uropepsin excretion during ACTH or cortisone administration approximating

TABLE II

Comparison of the Gastric Responses to ACTH Administration in Normals and After Vagectomy

	Normal	Vagectomy
Gastric pepsin (units/hr.)	186%	160%
Uropepsin (units/24 hrs.)	161%	198%
Free HCl (mEq./hr.)	241%	205%

150-200 per cent in 80 patients is presented in Table II, and is accompanied by a similar increase in acid and pepsin. Removal of the gastric antrum or vagectomy does not alter the gastric or uropepsin response to hormonal stimulation, as noted in Tables I and II.

The mean uropepsin output following ACTH or cortisone in vagotomized patients was 13,911 units; compared with 9,073 units in a control group whose vagi had not been severed. Peak response to ACTH or cortisone expressed as per cent increase in uropepsin rise is tabulated in Table II. It will be noted that vagectomized patients did not behave differently than did the control group receiving ACTH or cortisone.

Uropepsin Excretion as a Measure of Adrenocortical Activity:—The uropepsin response to adrenal stimulation with ACTH or the administration of the adrenal glucocorticoids, closely parallels the increase in 17-ketosteroid excretion. This was observed in 8 patients receiving ACTH for 2 to 10 days in

a daily dosage schedule of either 20 mg. of ACTH intravenously or 40 to 60 mg. of ACTH gel intramuscularly. Similarly 8 patients received daily doses of either cortisone 300-500 mg., Compound F 500 mg., or Compound B 50 mg. for periods ranging from 1 to 5 days. The peak response in uropepsin excretion very closely paralleled the peak increase in 17-ketosteroid excretion in both groups (Table III).

Statistical Correlation of Uropepsin and Adrenal Steroid Excretion:—Statistical evidence is presented correlating uropepsin excretion with the output of urinary 17-hydroxycorticoids and 17-ketosteroids in a. the normal state and b. normal subjects during exogenous ACTH stimulation.

Eleven normal subjects were studied daily in regard to their 24-hour urinary output of uropepsin, 17-hydroxycorticoids, and 17-ketosteroids for periods ranging from 8 to 44 consecutive days. From this data, correlation coefficients (r values) for each of these individuals were determined relating a. uropepsin to 17-hydroxycorticoids b. uropepsin to 17-ketosteroids c. 17-hydroxycorticoids to 17-ketosteroids. The correlation coefficients in these normal unstimulated males in respect to these three relationships varied widely from -0.15 to $+0.81$. In general, they tended to be of statistical significance, though of a low order of magnitude.

A similar degree of statistical correlation between the uropepsin and urinary 17-ketosteroid excretion in young men in the absence of specific adrenocortical stimulation has been shown by Garst and Hilliard[12].

Similarly, 3 normal male subjects were followed by daily uropepsin, urinary 17-hydroxycorticoid and urinary 17-ketosteroid studies before, during, and following stimulation of the adrenal gland with ACTH. In one case the ACTH (25 mg.) was administered intravenously over an 8-hour period daily for 5 days, while in the other two cases ACTH gel (40 units twice daily) was given for 5 days.

As noted in Table IV, where the data of one representative subject is tabulated, there was an immediate and parallel rise in the urinary output of uropepsin and the adrenal steroids following the initial ACTH stimulation, and this elevated excretion rate was maintained throughout the period of ACTH administration. The coefficient of correlation (r value) obtained in each of these cases for the period of ACTH stimulation was of a high degree of significance insofar as the uropepsin and 17-ketosteroid values were concerned, and is of a much greater magnitude than that found in the unstimulated subjects. The uropepsin-17-hydroxycorticoid correlation coefficients following ACTH stimulation tended to follow a similar pattern. Further analysis of these data, comparing the correlation coefficients for the normal unstimulated group with those obtained in the cases receiving ACTH, (using the weighted z relationship to integrate r values), gave definite statistical support to the observed parallel

increase in uropepsin and adrenal steroids under adrenocorticotrophin stimulation.

These statistical analyses would seem to suggest that in the normal state under conditions of normal adrenal function, the stomach was acting semiautonomously relative to the adrenal cortex. It can be inferred, however, that under conditions of ACTH-induced stress, the stomach, insofar as its pepsinogen production is concerned, comes more definitely under the influence of the adrenal cortex. The increased output of glucocorticoids produced by the ACTH stimulated adrenal gland, activates the peptic cells through a metabolic pathway still to be clarified, causing a greatly augmented pepsinogen production.

It is of further interest to note that the foregoing data comparing the correlation coefficients in normal men with and without ACTH, lend statistical support to Selye's "conditioned" theory of hormonal activity[13] and to Ingle's "permissive" concept[14]. Both investigators consider that the adrenal cortex has

TABLE III

COMPARISON OF UROPEPSIN AND 17-KETOSTEROID EXCRETION DURING THE ADMINISTRATION OF ACTH, CORTISONE, COMPOUND F AND COMPOUND B

	Number of Patients	Peak Uropepsin Response Increase	Peak 17-Ketosteroid Response Increase
Cortisone Compound F or Compound B	8	212%	164%
ACTH	8	312%	285%

a dual role in metabolic stress responses: the one role that of an agent which "permits" a metabolic response to occur, and without whose presence the response could not occur; and the second role casting the adrenal in a more directive position, with a positive relationship between the level of cortical hormone and the extent of secondary organ response. In applying this concept to the stomach, our data suggest that this organ enjoys a semiautonomous role relative to the adrenal gland under conditions of normal adrenal activity, although dependent on the presence of adrenal corticoids for normal peptic function. When the adrenal is stressed, however, a more integrated gastric-adrenal response ensues.

Uropepsin Excretion in Pituitary-Adrenal Dysfunction:—Indirect evidence favoring the hypothesis that gastric and adrenal activity are closely related, is derived from the study of uropepsin excretion and urinary steroid output in patients with hypofunction or hyperfunction of the adrenal and pituitary glands[15].

A markedly diminished uropepsin excretion was noted in patients with panhypopituitarism and Addison's disease, and a definite increase in uropepsin excretion was observed in patients with Cushing's disease, accompanied by parallel alterations in corticoid and ketosteroid excretion (Table V).

The mean of 12 patients with Addison's disease not receiving glucocorticoid replacement therapy was 542 units (S.E. ± 109), compared with the mean uropepsin of 3,670 units (S.E. ± 159) in 265 normal subjects. A similar reduction in steroid excretion was noted. A striking fall in output was also seen in 5 patients with panhypopituitarism who excreted a mean of 505 units, accompanied by a proportional fall in the steroid excretion similar to that observed in the untreated Addison's disease patients (Table V). A diminished mean

TABLE IV

MEAN RESPONSE OF UROPEPSIN AND 17-KETOSTEROID EXCRETION TO EXOGENOUS ACTH (A.M.—22-year old normal male)

Determination	Control (5 Days)	ACTH 40 u. Gel BID (5 Days)	Control (5 Days)
Uropepsin Units			
12 hours	1600	2393	1036
24 hours	3200	4786	2071
17 OH mg.			
12 hours	3.6	11.3	3.8
24 hours	7.1	22.5	7.6
17 Ks. mg.			
12 hours	10.6	19.3	12.6
24 hours	21.2	38.6	25.3

uropepsin excretion (365 units) was also found in 6 patients with decreased adrenal function secondary to myxedema. With specific stimulation of the adrenal gland with ACTH there was a prompt response in uropepsin output to normal or elevated levels. Hyperthyroidism *per se* does not significantly alter the uropepsin excretion (Table V).

In contradistinction to the hypoactive adrenal and pituitary states, in which the uropepsin excretion was markedly decreased, hyperactivity of the adrenal or pituitary (Cushing's disease) demonstrated in 12 patients, significantly elevated uropepsin excretion with a mean of 7,023 units, a rise of 100 per cent above the normal. The excretion of the urinary 17-hydroxycorticoids in this group averaged 23.5 mg. per 24 hours and the 17-ketosteroids 16.4 mg. per 24 hours (Table V).

It would appear that hyperfunction of the adrenal gland is associated with hyperfunction of the peptic glands, with the converse applying in states of adrenal hypofunction.

It is evident from these findings in patients with endocrine disease that an intact adrenal gland is essential for normal uropepsin excretion. The exceedingly low levels found in patients with Addison's disease and hypopituitarism, and the high values associated with adrenal and pituitary hyperactivity, further emphasize the significance of adrenal influences upon the stomach.

The glucocorticoids, such as cortisone, Compounds F and B, and meticorten are the only steroids which increase peptic activity. No uropepsin response was

TABLE V

UROPEPSIN EXCRETION IN ENDOCRINE DISEASES

Diagnosis	No. of Patients	Mean Uropepsin Excretion u/24 hrs.	17-Ketosteroid Excretion mg./24 hrs.	17-Hydroxy-corticoid Excretion mg./24 hrs.
Normal	265	3670	10.0-15.0	5.0-6.0
Addison's Disease:				
Untreated	12	542	3.8	1.0
Glucocorticoid replacement therapy	11	3412		5.0
Hypopituitarism:	5	505	3.7	1.5
ACTH replacement therapy	5	3701		
Cushing's disease	11	7023	16.4	23.5
Adrenogenital Syndrome	5	2512	20.8	5.0
Myxedema				
Untreated	6	365		
ACTH Stimulation	3	3675		
Hyperthyroidism	9	4420		

demonstrable after the prolonged administration of desoxycorticosterone, testicular and adrenal androgens, progesterone and potent estrogen preparations. The high levels of uropepsin in Cushing's disease, in which there is a known excess of 17-hydroxycorticoids, offer further evidence of the primary importance of the glucocorticoids in the gastric response. In adrenogenital syndrome, however, where there is an excess of adrenal androgens the uropepsin excretion was in the normal range (Table V).

The only pituitary hormone which induces a uropepsin response is adrenocorticotrophic hormone. Others such as growth hormone, thyrotrophic and gonadotropic hormone are ineffective.

Clinical Use of Uropepsin Excretion

The measurement of uropepsin excretion appears to be a useful adjunct in the evaluation of a number of gastrointestinal and endocrine diseases. A high level of uropepsin invariably signifies gastric hypersecretion and is highly suggestive of peptic ulcer disease. Values above 3,000 units were found in all patients with duodenal ulcer, regardless of the activity of the disease, and were encountered in 44.7 per cent of the normal group of 265 patients. A uropepsin output of greater than 3,000 units may also be encountered in gastric ulcer, ulcerating cancer, adrenal and pituitary hyperactivity, patients receiving ACTH or cortisone and patients under stress, such as that following surgery, burns, and severe pain[16].

Abnormally low levels of uropepsin output below 1,000 units have been encountered in patients with gastric cancer, pernicious anemia, Addison's disease, myxedema and total gastrectomy. It was encountered in only 2.6 per cent of normal individuals and was seen in only 1 of 90 patients with benign gastric ulcer.

In the presence of an ulcerating gastric lesion, a uropepsin excretion of 1,000 units or less indicates a high probability of malignancy, since only 1.1 per cent of 90 patients with benign gastric ulcer excreted less than 1,000 units. A urinary excretion of over 3,000 units favors, but does not prove a benign lesion, since 79.6 per cent of gastric ulcer patients excreted above this level in contrast to 21.7 per cent in the cancer group.

A low uropepsin *per se* would probably not be effective as a screening test for gastric cancer, since only 55 per cent of cancer patients excrete less than 1,000 units. It may be useful, however, in conjunction with other screening technics for gastric malignancy.

Uropepsin excretion appears to be of clinical value in differentiating duodenal ulcer from esophageal varices in patients with massive hemorrhage from the gastrointestinal tract. There is a distinct difference in the uropepsin excretion in the two groups in that patients with portal cirrhosis and esophageal varices excrete exceedingly low levels of uropepsin with a mean of 1,929 units compared with 9,444 units in patients bleeding from duodenal ulcer. In every instance of bleeding from duodenal ulcer the uropepsin values were greater than 3,500 units, while all patients with varices or cirrhosis of the liver demonstrated a low uropepsin below 2,125 units and in most instances were below 1,500 units.

Another sphere of clinical usefulness for the determination of uropepsin is in evaluation of patients who have undergone subtotal gastric resection, where gastric analysis is inherently difficult and often unreliable. In many instances, the uropepsin determinations would appear to indicate actively

secreting gastric tissue in patients presenting absent or low free acid upon gastric aspiration. This finding of low or absent gastric acidity may be attributed in part to intestinal reflux of biliary secretions.

The finding of a high uropepsin above 4,000 units in a patient with a previous subtotal gastrectomy, having recurrent symptoms is highly suggestive of a marginal ulcer. This is particularly pertinent since only 1 out of 21 patients with an uncomplicated gastric resection excreted more than 4,000 units. The mean of this uncomplicated postresection group was 2,775. In contrast to this, patients with marginal ulcer invariably excreted over 4,000 with a mean of 10,126 units. In general, the postoperative level of uropepsin is a reflection of the amount of functioning gastric mucosa remaining.

Comment

It is apparent from these and previous studies that adrenocorticotrophic hormone, by activating the adrenal cortex and releasing adrenal glucocorticoids, increases gastric secretion of acid and pepsin, and the urinary excretion of uropepsin[7] (Table II). This uropepsin response to hormone stimulation may be utilized as an index of gastric hypersecretion in patients undergoing treatment with prolonged ACTH or cortisone. The presence of a high output of uropepsin of 10,000 units or above, may serve as a warning of the impending complications of hormone therapy, such as ulcer formation, hemorrhage or perforation of the stomach.

The percentage increase in acid, pepsin and uropepsin during ACTH administration appears to be identical with or without vagotomy. Ulcer pain appears to be as easily induced by ACTH in patients with vagotomy, as in the nonvagotomized group. This ulcer pain is paralleled by a progressive rise in uropepsin to maximal levels, similar in magnitude to the active duodenal ulcer group. Furthermore, the response of the vagotomized patient to stress does not differ from that observed in an individual with intact vagi. The patient with a previous subtotal gastrectomy whose antrum has been removed, shows a similar uropepsin response to stress or adrenocortical stimulation. It would appear, therefore, that either acute or chronic physical stress may stimulate the stomach, independent of the vagus nerve and the gastric antrum, by way of a humoral mechanism involving the hypothalamic-pituitary-adrenal-gastric axis.

It is evident from the findings observed in patients with endocrine disease that an intact adrenal gland is essential for normal uropepsin excretion. The exceedingly low levels of uropepsin found in patients with Addison's disease and hypopituitarism, as well as the high values associated with adrenal and pituitary hyperactivity, further emphasize the significant role played by the adrenal gland in affecting uropepsin output.

It is of some interest that only steroids of the so-called glucocorticoid type, such as cortisone and Compounds F and B, appear to activate the peptic cells to increase pepsinogen synthesis. An increase in gastric secretion and uropepsin excretion in the normal subjects and restoration of the uropepsin excretion to normal levels in patients with Addison's disease and panhypopituitarism can only be produced by these steroids. No uropepsin response is demonstrable after prolonged administration of desoxycorticosterone, testicular and adrenal androgens, progesterone, and potent estrogen preparations. The high levels of uropepsin in Cushing's disease, where there is a known excess of corticosteroid excretion is further evidence of the primary importance of the glucocorticoids on uropepsin response.

The close relationship found between the increase in uropepsin excretion and 17-ketosteroids during hormone therapy and accompanying states of hyper- and hypoadrenal cortical function suggest the possibility of utilizing the uropepsin determination as an index of adrenal responsiveness. A positive correlation has been observed in normal males aged 17 to 40 between uropepsin and urinary 17-ketosteroid excretion[12]. The similar parallel fluctuation observed in this study tends to confirm their results and further emphasizes the sensitivity of the peptic cells to changes in circulating corticoids.

The low uropepsin output in myxedema appears secondary to the associated depression of adrenal function occurring in states of marked hypothyroidism. With specific stimulation of the adrenal with ACTH, there was a prompt response in uropepsin output to normal or elevated values within one day, despite little or no increase in general metabolism.

Conclusions

The determination of uropepsin excretion has proven of clinical value in the differential diagnosis of certain gastrointestinal and endocrine diseases, and as a measure of gastric secretory activity and adrenal function.

A high output accompanied peptic ulcer disease, adrenal and pituitary hyperactivity (Cushing's disease) and states of acute and chronic stress; and occurred in patients receiving ACTH or cortisone therapy.

Low or absent levels characterized pernicious anemia, adrenal and pituitary hypofunction (Addison's disease and panhypopituitarism) myxedema, total gastrectomy and a majority of cases of gastric carcinoma.

The uropepsin excretion is not suitable as a screening test for gastric cancer, since only 55 per cent of patients with cancer excreted less than 1,000 units. In the presence of an ulcerating gastric lesion a uropepsin excretion of 1,000 units or less indicates a high probability of malignancy, and a high level above 3,000 units favors, but does not prove a benign lesion.

The level of uropepsin may be of considerable value in differentiating duodenal ulcer from esophageal varices as a cause of massive hemorrhage from the upper gastrointestinal tract.

The measurement of uropepsin offers a convenient means of evaluating gastric secretion in the postgastrectomy patients without the necessity of intubation. High levels in these patients suggest marginal ulcer.

Vagotomy does not appear to alter the uropepsin excretion or the uropepsin response to adrenal cortical stimulation.

The close relationship between the increase in uropepsin excretion and urinary 17-ketosteroids during adrenal stimulation and hormone therapy suggests the possibility of utilizing the uropepsin output as an index of adrenal responsiveness. The exceedingly low levels of uropepsin in patients with Addison's disease and panhypopituitarism, and the high values in patients with adrenal and pituitary hyperactivity, paralleled by similar patterns of urinary corticoid excretion, emphasize the significance of adrenal activity in uropepsin excretion.

The development of epigastric pain, reactivation, or production of peptic ulcer, with hemorrhage or perforation, following the administration of ACTH and cortisone, is invariably accompanied by a considerable increase in gastric secretion of acid and pepsin and excretion of uropepsin. An elevated uropepsin during prolonged hormone therapy may antedate these complications and is of considerable value in the management of these patients.

These studies support the concept that acute and chronic stress stimulate the stomach and increase uropepsin excretion by way of a humoral mechanism involving the hypothalamic-pituitary-adrenal-gastric axis, independent of the vagus nerve or the gastric antrum.

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PHRENIC NERVES AND GASTROINTESTINAL MECHANISMS. LEFT PHRENIC CRUSH AND VAGOTOMY*

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Anatomically the left phrenic nerve is distributed to the diaphragm only and is divided into three parts, anterior, posterior and lateral. The right phrenic nerve has an anterior lateral and posterior lateral distribution to the diaphragm, a third branch pierces the diaphragm and innervates the celiac plexus, from which branches are supplied to the biliary and gastrointestinal system[1]. Other branches go to the so-called phrenic ganglion.

A chance observation by Noack[2] that patients with tuberculosis, subjected to left phrenic exeresis showed rapid gastric emptying, led us to study the effects of both phrenic nerves in gastrointestinal mechanisms.

The following operations were performed on dogs: left phrenic section[3], left phrenic section and vagotomy[4,5,6], right phrenic section[7], bilateral phrenic section, and vagotomy with uni- or bilateral phrenic section[8].

Finally the results of our animal experimentation encouraged us to apply certain procedures to surgical cases of peptic ulcer in whom vagotomy was performed.

The experimental methods have been described previously in the papers quoted above.

Results

Animal Experiments:—In the dog, left phrenic section above the diaphragm shortened gastric emptying considerably. The stomach assumed a forward position, and an unusually large gas bubble was present. Left phrenic section with bilateral vagotomy above the diaphragm alleviated most of the complications associated with vagotomy alone. There was no cardiospasm, gastric stasis, vomiting, diarrhea, or gastric dilatation.

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Right phrenic section with vagotomy did not produce changes in gastrointestinal mechanisms, but bilateral phrenic section with vagotomy was fatal in all of five experiments. Right phrenic section alone caused the duodenal bulb to be elevated as high as the cardia, and much gas was present in the stomach. The gallbladder was appreciably elevated, yet no change in gallbladder filling nor in gastric and gallbladder motor functions was seen.

Bilateral phrenic section caused considerable gastrointestinal gaseous distention. Stomach and duodenum moved forward considerably, yet there was no appreciable change in motor function.

Phrenicotomy in Man:—Our results with left phrenic section and vagotomy in the dog encouraged us to employ left phrenic crush in man as an adjunct to surgery for peptic ulcer. The results on 12 patients are presented in Table I. All of the 12 cases suffered from duodenal ulcer with varying degrees of gastric retention. In all instances, the left phrenic nerve was crushed in the neck during the abdominal operation. Vagotomy was performed subdiaphragmatically and care was taken to cut all branches. Posterior gastrojejunostomies were done, and subtotal gastrectomy included approximately two-thirds of the stomach. Postoperatively, Wangensteen suction was used although we felt that it was not necessary, because no gastric dilatation or retention was evident in any one of the cases. Case 9 removed the stomach tube on the second postoperative day and refused reintroduction, but nevertheless no complications occurred. We feel, however, that the presence of the Wangensteen tube may prevent complications in certain instances.

In nine patients (Cases 3 to 11) left phrenic crush, subdiaphragmatic bilateral vagotomy and posterior gastrojejunostomy were performed. In Case 12 in whom a considerable degree of gastric retention and pyloric obstruction existed, left phrenic crush, subdiaphragmatic vagotomy and subtotal gastrectomy were performed. In two patients (Cases 1 and 2) left phrenic crush and subdiaphragmatic vagotomy were used without a gastric shunting operation. The results in these two patients were equally as good as in the rest of the group in whom a shunting operation was performed.

The postoperative course in 10 patients was "excellent" and no complications were observed. In the two patients with a "good" postoperative course, complaints and complications occurred which were not necessarily related to the operation. Case 7 had been suffering for years from adhesions following multiple lower abdominal operations, she was a severe psychosomatic case and a demerol addict. Case 8 was suffering from heart disease to which she succumbed at home 12 days postoperatively.

All 12 patients were ambulated on the second postoperative day, they left the hospital within one week after operation (except Case 12 who for social reasons stayed two weeks) and they were back to work within six to eight

TABLE I

LEFT PHRENIC CRUSH IN SURGERY FOR DUODENAL ULCER

Case No.	Patient	Age	Sex	Complaints Years	Complications	Type of Operation	Postoperative		Years Since Operation and Follow-up
							Course	Complications	
1	H.J.	28	M	5	Retention, adhes. to gallbladder	L. phren. crush, s. diaphr. vagot.	Excel.*	None	3, works, no recurr.
2	S.R.	55	M	5	Retention	Same	Excel.	None	3, works, no recurr.
3	W.S.	61	M	½	Retention	L. phren. crush, s. diaphr. vagot., gastrojejunost.	Excel.	None	6, works, no recurr.
4	L.H.	37	F	1-2	Retention	Same	Excel.	None	6, works, no recurr.
5	W.S.	49	M	½	Retention Hemorrhage	Same	Excel.	None	1, works, no recurr. bladder cancer.
6	E.R.	71	M	1 week	Retention	Same	Excel.	None	No follow-up
7	C.L.	38	F	18	Retention	Same	Good†	Old adhesions (hysterect.) demerol addict	4, works, no recurr.
8	L.L.	60	F	20	Retention	Same	Good	Myocarditis	12 days postop.
9	L.F.	37	M	5	Retention	Same	Excel.	None	2, works, no recurr.
10	C.A.	48	M	5	Retention	Same	Excel.	None	5, works, no recurr.
11	N.K.	42	F	20	Retention	Same	Excel.	None	5, works, no recurr.
12	J.B.	63	M	5	Retention	L. phren. crush, vagot., s. gastrect.	Excel.	None	4, works, no recurr.

*Excellent denotes: patient out of bed 2 days postoperatively, left hospital within 1 week, was back at work within 6-8 weeks.
†Good denotes: some complaints postoperatively, not necessarily connected with operation.

weeks postoperatively. With the exception of one case which was lost, the patients were followed from one to six years postoperatively, with an average of 3.9 years. In none of them did ulcers recur, nor were there complaints referable to ulcer or to the operation.

We feel that the results of combined phrenic crush and vagotomy with or without gastric shunting operations are excellent when indicated, and we submit them to the profession for serious consideration. We cannot explain the mechanism by which left phrenic section shortens gastric emptying time and has such beneficial effects in abolishing the gastric retention, diarrhea, etc., which are seen so often following vagotomy alone. The appearance of a larger gas bubble than normal and straightening with possible shortening of the distance between cardia and pylorus were two objective observations which, however, do not contribute much to an explanation of the shortening of gastric emptying time and the smooth course of patients and dogs following vagotomy.

We have used left phrenic crush in a case of bleeding and painful diaphragmatic hernia in an aged woman in whom surgical repair was not feasible. In this patient, bleeding and pain stopped immediately, but when recovery of the crushed phrenic nerve took place, the former symptoms recurred, and phrenic exeresis had to be performed. Following this, all symptoms disappeared and the patient has been without complaints for the last six years. In the cases with the combined operations for peptic ulcer, regeneration of the left phrenic nerve which occurs usually within a few months after crushing, did not seem to play any role clinically. In the case of persistent hiccough which could not be suppressed by any of the known medical treatments, bilateral phrenic crush in the neck abolished the hiccough and was not followed by any serious complications.

In the dog, cardiospasm occurred following section of both vagus nerves below the hilum of the lungs, and it was abolished by left phrenic section. This observation was applied by our associate, Dr. C. Phillips, in patients with chronic achalasia of the cardia, in whom left phrenic crush was followed by disappearance of the achalasia, ability to eat without disturbance and gain in weight[5].

Summary

Left phrenic section was followed by faster gastric emptying time in man and in the dog.

In man, as well as in the dog, left phrenic crush or section abolished the gastric distention and retention usually observed following vagotomy.

Results of operations on 12 patients in whom phrenic crush was added to subdiaphragmatic vagotomy, subdiaphragmatic vagotomy and gastrojejunostomy and subdiaphragmatic vagotomy and subtotal gastric resection, are reported.

In experiments on the dog, the effects on gastrointestinal mechanisms of unilateral and bilateral phrenicotomy alone or combined with unilateral or bilateral vagotomy were explored.

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TWO CASES OF CARCINOMA OF THE STOMACH SURVIVING AFTER SURGERY MORE THAN TWELVE AND EIGHT YEARS RESPECTIVELY

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In recent years a great deal of advancement has been made in the general management of surgical cases. Most of the operative progress has been noticed in the field of gastric cancer by an increase in the number of cases in which the growth can be removed and the mortality rate reduced. Yet, the improvement in the long term survival has been very little. By the time the patient seeks relief from symptoms and has gone through the diagnostic procedures, extension and/or dissemination of the lesion has already made it incurable in most of the cases. It is in these cases that there are differences of opinion as to whether the patient should be submitted to surgery or not.

We are therefore reporting two patients with carcinoma of the stomach who were treated by subtotal gastric resection. Both are well at present, one more than 12 and the other more than 8 years without any abdominal or gastric complaints.

Case 1:—A. S., age 63, white, male, was first seen at the gastrointestinal clinic of the Cumberland Hospital, Brooklyn, N. Y., on December 5th, 1940. The patient was complaining of epigastric pains that would come on about one-half to three hours after meals. Occasionally the pains would awaken him at night. Appetite was fair and bowels moved without the aid of laxatives.

Past history was essentially negative.

Laboratory data:—Blood serology was negative. Complete blood count, urine as well as gastric analyses were reported to be within normal limits. Radiographic studies of the gastrointestinal tract were interpreted as essentially normal. Cholecystographic examination revealed a gallbladder of good concentration and delayed evacuation.

The patient was treated conservatively with proper diet, antispasmodics and sedatives. His condition, however, deteriorated.

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In December 1942, a roentgenographic study of his gastrointestinal tract revealed a filling defect in the midportion of the body of the stomach suggestive of malignancy.

The patient was admitted to the hospital on January 23rd, 1943, and a subtotal gastrectomy was done.

The pathological report was that of adenocarcinoma.

The postoperative course was uneventful. The patient was discharged from the hospital on February 25, 1943, and has been followed in the gastrointestinal clinic since then. He has been well except for occasional sour eructation and bloated feeling after meals. His appetite is good and he has gained 21 lbs.

Radiographic studies of the gastrointestinal tract on various occasions from July 1943 to February 1953, were interpreted as evidence of subtotal gastric resection with possible malignant infiltration along the greater curvature of the stomach in the *pars media*. Because of the x-ray interpretations, the patient was advised to have hospitalization and/or gastroscopic examination both of which he refused.

A gastric analysis in June 1951, revealed free HCl—5 units and total HCl—60 units. Blood count was reported as 5 million red blood cells and 100 per cent Hgb.

Roentgenologic studies of the gastrointestinal tract in February 1953, were for the first time interpreted as indicating no intrinsic gastric or duodenal defects. A follow-up study done in April 1954, however, was reported as revealing possible gastric ulcer on the lesser curvature. A recheck, using spot radiography, in May 1954, was interpreted as showing no intrinsic defect of the stomach.

The last x-ray studies of the gastrointestinal tract done in February 1955, were reported as showing no intrinsic gastric or duodenal defects.

Comment:—In this case radiographic studies of the gastrointestinal tract did not indicate any gastric lesion until two years after the first x-ray examination of the stomach was done.

It is well known that with the combination of all diagnostic procedures, about 15 per cent of the early cases are still not diagnosed.

Repeated roentgenologic studies of the gastrointestinal tract done during the first postoperative ten years were reported as indicating recurrent malignant infiltration of the resected stomach. In the past two years, however, radiographic studies of the stomach were interpreted as revealing no intrinsic gastric or duodenal defects.

Case 2:—F. B., age 65, white, male, was first seen in the gastrointestinal clinic of the Cumberland Hospital, Brooklyn, N. Y., on April 13, 1944, complaining of abdominal pains pointing to the right upper quadrant radiating to

the back. The pains were dull and at times relieved by food and/or medication. Appetite was good and bowels moved daily. The patient claimed that he had lost some weight in the past year.

Past and family histories were irrelevant.

Physical examination was negative except for a sense of resistance in the right hypochondrium.

The clinical impression was that of gallbladder pathology and questionable gastric malignancy.

Laboratory data:—Gastric analysis revealed free HCl—0 and total HCl—65 units. Blood and lactic acid were present. Stool examination for occult blood was positive.

Cholecystographic examination revealed a gallbladder of good concentration and delayed evacuation.

Radiographic studies of the gastrointestinal tract gave negative results. A recheck at a future date, however, was advised by the x-ray department.

The patient felt better on medical therapy and did not return to the clinic until April 3, 1947. At this time he complained of epigastric pains of two months' duration. The pains would come on before meals and radiate to the back. Appetite was fair and bowels moved daily.

X-ray studies of the gastrointestinal tract done in June 1947, revealed a persistent defect involving the *pars media* and *pars pylorica*, indicative of malignant infiltration. A re-examination of the gastrointestinal tract six days later was interpreted as an organic defect of the greater curvature on the antrum, probably adenocarcinoma. At that time abdominal palpation revealed a mass in the epigastrium.

Subtotal gastrectomy was performed and the pathological report was adenocarcinoma of the pylorus with an ulcerating area. No metastases were seen or found grossly. The recovery was uneventful and the patient has been followed in the gastrointestinal clinic since his discharge from the hospital on July 30, 1947.

At times the patient would complain of a sense of fullness after meals and occasional abdominal discomfort. His appetite remained good and he gained weight.

In May 1948, the blood count revealed 4.1 million red cells and 81 per cent Hgb. The stool was negative for occult blood.

Radiographic studies of the gastrointestinal tract done in October 1948, revealed evidence of a subtotal gastrectomy. There was a defect near the stomatous region, as well as the adjoining small loop of the intestine. A re-examination in February 1949, however, was reported as essentially negative.

X-ray studies of the gastrointestinal tract made in June 1949, revealed a suspicious small ulcer niche on the lesser curvature of the upper part of the *pars media*. A recheck four months later did not show the above described ulcer niche.

On April 4, 1952, the patient was admitted to the hospital with complaints of general weakness, abdominal pains and diarrhea of one month duration. Physical examination was negative.

A study of the colon by barium enema done on April 17, 1952, was reported as negative for pathology. Radiographic studies of the gastrointestinal tract made on April 23rd, 1952 revealed evidence of a resected stomach, otherwise no demonstrable pathology. Other laboratory data were as follows—red blood cells 4.39 million, Hgb. 81 per cent, white blood cells 9.100 with a normal differential. Blood chemistry—urea nitrogen 15 mg. per cent and sugar 74 mg. per cent. Klein was negative. Stools were negative for occult blood and the urine examination was negative. Gastric analysis revealed free HCl—5 units and total HCl—16 units.

The patient did well on proper diet and was discharged from the hospital to be followed at the gastrointestinal clinic.

A roentgenological study of the gastrointestinal tract done on November 5th, 1953, was interpreted as partial gastrectomy with a normally functioning stoma. There was suggestion of malignant infiltration on the posterior wall of the gastric pouch. A repeated study a month later was again reported as suggestive of malignant infiltration of the gastric stump. The patient felt better, however, than at any time before and refused hospitalization.

X-ray studies of the gastrointestinal tract done on August 30th, 1954, and on February 24th, 1955, were both times reported as a subtotal gastrectomy with a normally functioning stoma and no evidence of malignant infiltration.

Comment:—In this case radiographic studies of the gastrointestinal tract done during the patient's first visit to the clinic were interpreted as negative and a recheck was advised. The patient, however, did not report to the clinic for three years. When the patient did return to the clinic, physical examination revealed a palpable mass in the epigastrium and the stool examination was positive for occult blood. At this time two x-ray studies of the gastrointestinal tract were reported as showing malignant infiltration of the stomach involving the *pars media* and *pars pylorica*.

Here again, as in the first case, postoperative radiographic studies of the gastrointestinal tract on various occasions were interpreted as revealing recurrent malignant infiltration of the resected stomach. Repeated studies in the past two years however, were reported as negative.

Discussion:—Swymertan and Truelove[1] reported on 375 patients with carcinoma of the stomach who were treated at the Radcliffe Infirmary in Oxford from

1938 to 1949 inclusive. Complete follow-up data were obtained in all cases. Laparotomy was carried out in 63 per cent and resection of the growth in 30 per cent of the cases. Five and six-tenths per cent of the total number of patients followed over a five-year period remained alive. Twenty-three per cent of the resected group were alive after five years, while only .7 per cent of the nonresected group survived for more than five years.

The important finding of this study was the prognostic significance of the length of the history, which showed that a long history indicated that the neoplasm was of the slow growing type. Our two cases seem to confirm their theory that the longer the preoperative history of the patient with gastric cancer, the better the postoperative prognosis, when the growth is still suitable for resection.

Balfour[2] reported that patients with a history of less than six months who survive resection have a five-year survival rate of 25 per cent, whereas patients with a history of more than one year have a five-year survival rate of 35 per cent.

Haas[3] recently reported two cases, with symptoms of more than two years' duration with palpable masses in both patients which were resected and have been doing well ten years after the operation.

Pack[4] reported two cases of gastric carcinoma resected 20 years ago and both are still living. One patient had a history of about one and a half years preoperatively. The second patient had no complaints at all. The gastric lesion was found on routine x-ray studies of the gastrointestinal tract.

This does not mean that an early diagnosis is of little importance. On the contrary, every effort must be made to shorten the time between the onset of symptoms and the final diagnosis. Cases of gastric cancer of long standing, however, and even with palpable masses, as in our second case, should not discourage us from advising surgery.

Summary

1. Two cases of gastric resection for carcinoma, who have remained for more than 12 and 8 years respectively without recurrence, are recorded.

2. In one case 2 years elapsed from the time the patient was seen to the time of the operation. In the second case there was a 3-year preoperative history and a palpable epigastric mass before surgery.

3. The conclusion to be drawn from such cases is that exploratory laparotomy and gastric resection for cancer of the stomach should be done irrespective of a long standing history and/or palpable epigastric mass.

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NEWER TRENDS IN CAUDAL ANESTHESIA*

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INTRODUCTION

During the late 1930's, due to the efforts largely of Dr. Robert Hingson[1] who popularized caudal anesthesia in obstetrics, and due to the efforts of Dr. John Lundy[2] of the Mayo Clinic in behalf of this technic in pelvic work of all types, caudal anesthesia became an accepted part of the armamentarium of all people in producing anesthesia of the pelvic area. A great percentage of the work was done not only by the caudal approach, but it was reinforced usually by a transsacral block as well, creating a sacral block or sacral anesthesia. The agents then were primarily procaine and Metycaine®†. The technic, even in the hands of the most skilled individual, had a percentage of failure of approximately 5 per cent. In many instances the onset was slow and it was not unusual at all to have the onset of surgical anesthesia require half an hour wait after the injection of the anesthetic agent. The duration was variable and in many instances the anesthesia was not as uniform as one may have desired; it occasionally was spotty. The technic, however, was safe and few complications of any severity were reported in the hands of workers who did relatively few as well as in the hands of those whose series numbered among the thousands.

The technic then, as today, caused little disturbance to metabolism. Headaches as a result of this technic were virtually unknown. It required little in the way of extra equipment and basically the rather unusual postures utilized by some surgeons during their various procedures, caused less physiologic disturbance with this form of anesthesia than would be caused with most other varieties. All in all, it represented very close to the ideal for work in and about the anorectal area.

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†Metycaine®—Trade name of gamma-(2-methyl-piperidino)-propyl benzoate hydrochloride, manufactured by Eli Lilly and Company, Indianapolis, Ind.

The slowness of onset, however, the spottiness of the anesthesia, the relatively high percentage of failures, the short duration and other similar phenomena that result from the use of the weaker agents, were troublesome and tended to prevent the increase in the usefulness of this technic.

Caudal Anesthesia Today

Today, due to the efforts on the part of the pharmacologists, we have had made available to us many more potent agents which have, to a great degree, eliminated many of the undesirable factors associated with caudal anesthesia. In general, these agents are the more potent agents, such as Xxylocaine®‡ or lidocaine, Pontocaine®§ or tetracaine, CyclaineF** or hexylcaine, and/or combinations of these drugs. With these drugs there has gradually been an abandonment of the sacral block in preference for the single needle caudal approach for most anesthetics of the anorectal area. Gradually, shorter needles have been used rather than the long, standard caudal needles. The onset of anesthesia has markedly increased in speed. The duration of anesthesia has also increased and spottiness is now a rare phenomenon. The safety of the technic seems still to be as good as when the so-called less toxic agents were used. One should, however, exercise much more caution than was previously utilized when using agents such as Pontocaine, Xylocaine, Cyclaine, etc. These agents are frequently used in concentrations and in total dosages which could result in death if the precautions so carefully set forth by Dr. Lundy and Dr. Hingson are not followed. Total spinal anesthesia could easily result from perforation of the lower dural sac and with the longer lasting or more potent agents, much more intense and widespread anesthesia than is desired may result. It is to be expected also that the reactions to local anesthesia will occur somewhat more frequently with these agents. The exact difference in the incidence of complications to be expected, cannot, however, be prophesied in that the true toxicity or the true complication incidence cannot be based upon experimental work of the pharmacologist in the laboratory on the usual laboratory animals. All of the newer anesthetic agents must be tried after the laboratory animal studies seem to indicate that the study is justified, and only after literally tens of thousands of cases have been carried out, can one begin to make a correct evaluation of the safety and the value of any of the newer agents that have been suggested for clinical trial.

Xylocaine, Pontocaine and Cyclaine are three of the agents which now have the greatest popularity for the creation of caudal anesthesia. These three

‡Xylocaine®—Trade name of lidocaine, manufactured by Astra Pharmaceutical Products, Inc., Worcester, Mass.

§Pontocaine®—Trade name of tetracaine, manufactured by Winthrop Laboratories, Inc., New York, N. Y.

**Cyclaine®—Trade name of hexylcaine, manufactured by Sharp and Dohme, Philadelphia, Pa.

agents might well be classed as newer agents. Although Pontocaine or tetracaine has been known a long time, its popularity from the standpoint of injection anesthesia has only occurred in the last few years.

The recent popularity of Pontocaine in block anesthesia is due to the excellent work of Dr. Daniel C. Moore[3] and Dr. John Bonica of Seattle and Tacoma. They showed quite conclusively that Pontocaine in approximately 0.15 per cent concentration, may be used for block anesthesia in almost all areas of the body where the medium-sized nerves exist. The onset of anesthesia is moderately rapid although occasionally one sees a slight delay in onset. When the solution is warmed and carefully injected, however, this delay is not too frequent. The duration is extremely long; in fact, at times when epinephrine is added, it is not unusual for anesthesia to persist for periods of six to eight hours. In some instances this may be an advantage and in others a disadvantage. Certainly in their hands, in the hands of most other skilled individuals, the disadvantages from Pontocaine are relatively slight. Primarily these are a relatively poor spread, an inherent fear of toxic reactions based on previous concepts more than actuality, but basically this agent today is rightfully one of the most popular local anesthetic agents in America.

Another agent extremely popular and of more recent vintage is Xylocaine[4] or lidocaine. This agent produces a fairly rapid onset, an excellent spread, a rather good duration, good relaxation and all in all, is an excellent local anesthetic agent. There is a misunderstanding, however, on the part of many as to its potential toxicity. The comparison of this agent with procaine has led many to believe that in reality one can use approximately half of the amount of Xylocaine as one uses of procaine. This view is not shared by many leading anesthesiologists. Undesirable reactions have occurred when using Xylocaine. Primarily, these reactions have been the central nervous system depression-stimulation types of toxicity reactions. In a few instances, the more severe reactions have occurred, but when one considers the tremendous amount of this agent that is being used today and being used somewhat carelessly by many, one realizes the relative safety of even this agent. Xylocaine is an extremely good agent for the individual whose technic tends to be a little more careless in that he will get a greater incidence of good anesthesia. Carelessness, however, may also breed more accidents. This agent is an excellent agent to be used with the previously mentioned Pontocaine in order to aid in the onset and in the spread of the combination. In all probability, a mixture of 0.075 per cent Pontocaine and 1 per cent Xylocaine is one of the most popular anesthetic agents in America today. One wonders as to the actual toxicity of this combination. Certainly it is not unreasonably frequent. Many more years of experience with this combination must accrue before its true toxicity can be evaluated.

Cyclaine[5], recently introduced, has been gaining increasing popularity. This agent, although not quite as potent as the previously mentioned agents, is also

fairly rapid in onset, spreads nicely, provides good duration, and would seem to be less toxic. On four occasions, however, we have seen that when this drug was injected with epinephrine into the skin, it has caused undesirable skin irritation. It is interesting that the irritation that has occurred in deeper tissues has been far less frequent than with the other anesthetic agents. This agent in the skin seems to be a little more toxic than is popularly claimed; but systemic toxicities are extremely rare.

The toxicity and the value of all these agents are of such high degree that were I to require an anesthetic, there would be no hesitancy on my part to

TABLE I

SUMMARY 100 CASES CAUDAL ANESTHESIA UTILIZING SYMPOCAINE 0.5%

		Range		
	Average	Lowest	Highest	Comment
Dose	109 mg. (21.8 c.c.)	40 mg.	350 mg.*	
Onset	4½ mins.	10 sec.	12½ min.	
Duration	123 min. (2 hr. 3 min.)	35 min.		2 cases less than 60 min. 7 cases over 200 min.
Failures	2 failures to produce anesthesia 1 level T9—level necessary T5			
Side-effects	3 hypotension (systolic fall 180 to 110) 140 to 104) 110 to 60) 2 drowsiness 1 postoperative nausea 4 stinging on injection (average 10 sec.) 1 local erythema 11 Total			

*Missed initial injection. Repeat injection successful.

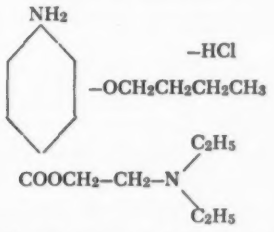
have utilized upon me any of these agents. Attention, however, to the details of such things as testing for intravascular injection, being sure that one's needle is distal to the dura, slow, careful injection utilizing the correct maximum concentration and quantity, must be carried out. If this is done, reactions to these agents are relatively rare. True, the more potent the agent the more frequently one should see reactions to the agent. It must be taken into consideration, however, that if one correctly dilutes and uses lower concentrations of these agents, the increased toxicity on a milligram per kilogram of tissue basis may markedly be diminished and be actually less toxic from a clinical aspect.

Present Study

Approximately one year ago, WIN-3706 or Sympocaine[®][6,7] which is a derivative of procaine (it is actually a butoxy substitution on the second carbon atom of the procaine molecule), was made available to us at the Hines and Westside Veterans Hospitals and the University of Illinois for study. Approximately 1,000 spinals have been done using this agent and several hundred blocks have been carried out using Sympocaine. This agent had properties that seemed to justify its use in caudal anesthesia. Therefore an appropriate worksheet was constructed and all of the residents and staff were asked to use Sympocaine in place of the other popular agents from time to time, making out a complete worksheet with each case. The results accrued in the first 100 caudal anesthesias are so interesting as to deserve a cursory or preliminary report.

In the 100 cases studied with Sympocaine in a 0.5 per cent concentration without epinephrine, the following results were found.

Formula of Sympocaine



1 Diethylaminoethyl–4 Amino–2 Butoxy Benzoate Hydrochloride ($C_{17}H_{28}N_2O_3$. HCl)

1. *Dosage:*—The mean dosage was 20 c.c. of 0.5 per cent or 100 mg. of Sympocaine. The average, however, was 109 mg. or 21.8 c.c. The variation was from 40 to 220 mg.

2. *Duration:*—The mean duration was approximately 123 minutes with a low of 35 minutes and a high of over 200 minutes of actual anesthesia. There were only 2 cases that had anesthesia less than one hour.

3. *Onset:*—The average onset was 4¼ minutes or a mean of 5 minutes. The onset was 10 seconds from the time of the withdrawal of the needle to a maximum of 12¼ minutes.

4. *Failures:*—There were 3 cases of failure. Two of these were instances in which no anesthesia resulted, probably due to a technical or anatomical variation, and one instance in which the level attained was the ninth thoracic vertebra when in reality for the operation that was accomplished, a T5 level was necessary.

5. *Side-effects:*—There were 3 cases of hypotension, all without sequelae, all responding to moderate doses of vasopressors. There were 2 cases of drowsiness that required no treatment, 1 case of postoperative nausea, 4 cases of stinging on injection that lasted approximately 10 seconds, and 1 instance of local erythema at the needle site. None of these side-effects required any unusual treatment nor were there any sequelae as a result.

This study, in its preliminary nature, is reported only for the purpose of noting some rather interesting data. For example, one sees already in the first 100 cases, 2 instances of drowsiness to remind one of the trouble occasionally seen with Xylocaine, a little local irritation in the skin to remind one of the Cyclaine, the speed, potency and duration to remind one of Pontocaine. We, however, take the liberty of reporting this study for certain reasons. These reasons are that other blocks have been done with this agent and as data accumulates daily, we become increasingly encouraged in our efforts in behalf of our study of this agent in that the data would tend to substantiate the excellent animal pharmacology done by Dr. F. P. Luduena[7]. Also, it is hoped that other workers having greater facilities for study of this agent may be encouraged to carry on careful studies along this line.

At this time, it can be stated that this agent, although seemingly of a more toxic group, did not cause any serious reactions. But, it must be emphasized that before an opinion can be formed as to its potential toxicity, more than 10,000 cases must be carried out and the results compared to the other commonly employed technics. We feel encouraged, however, by our preliminary review of this agent, in its use in spinal anesthesia, regional anesthesia of varying types among which is included caudal anesthesia. It seems to us at present that the agent is rapid acting, good spreading, of fairly good duration, having relatively little toxic side-effects. Our greatest fear at the present time, however, is that more caution must be utilized in the use of this agent than with the older, less potent agents. Time may prove, however, that this fear is entirely ungrounded. It is hoped that with the use of smaller total volumes and lower concentrations, that the comparative toxicity of this agent and the commonly employed agents may be essentially the same. If this is so, then certainly the more rapid onset and the more uniform spread, the better duration, will justify the greater use of this agent.

In direct contrast to the data presented here, there has been a great deal of work done by Dr. F. F. Foldes[8] of Pittsburgh on another new agent 2-chloroprocaine*. This drug approaches the problem from another aspect. One here is dealing with a drug that is much more rapidly metabolized. Its effectiveness is approximately that of procaine but it seems to have a better spread and a more rapid onset with what would logically seem to be a diminished danger

*Halestyn Hydrochloride, Wallace and Tiernan.

of reaction because of its rapid metabolism. This rapidity of metabolism of the drug may eventually necessitate concentrations of 3 per cent in order to get good relaxation in a very high percentage of the caudal anesthesia cases. The drug is as yet too new for a complete crystallization of opinion. Although we have done no cases ourselves, judging from the reports of others, it offers a great deal of hope for the betterment of caudal anesthesia.

In summary it may be stated that with the introduction of the newer anesthetic agents, anesthesia of the pelvic area by the use of the caudal technic has withstood the test of time. With these newer agents, the onset of anesthesia has been markedly increased in its attainment, the duration has been lengthened or at least held fast, the spreads have been more uniform, failures are gradually decreasing. This technic requires an attention to anatomical and pharmacologic details to make it the ideal anesthetic technic for anorectal surgery.

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GLUTEN SENSITIVITY

SPRUE—?

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It is an accepted fact that some people are sensitive to various foods, and that different individuals respond to the same food in diverse ways. It has not yet been widely accepted in this country, however, that the protein of wheat and rye (gluten) can be responsible for a series of symptoms which may have its inception in childhood (celiac disease) and go from there, perhaps years later, to a group of symptoms which we know as sprue syndrome. The glutens are a combination of proteins composed of gliadin, glutelin, and perhaps mesonin, each of which may be composed of subgroups.

Case 1:—A 53-year old, white, male physician who, except for measles in childhood and influenza in 1918, considered himself in good health. In retrospect, he remembers a number of bouts of diarrhea but attributed them to fatty foods. In April 1951, he was suddenly seized with a diarrhea that was to result in a loss of 40 pounds within three weeks. Up to the age of 34 he could not get above 125 pounds; after that his weight increased to 155. The drop brought it down to 115, and now, 5 years later, it is about 140. He always had had a "pot belly" with thin arms, legs, face and chest. With the weight loss there was general weakness, including voice weakness. Before the onset of the severe liquid diarrhea, there was a period of 3-4 months of foul bulky stools. The peculiar odor was noted especially by his family from the onset. Examination at this time was negative except for the tense "pot belly". A colon x-ray was negative. A gastrointestinal series demonstrated the small intestinal pattern of sprue; a sugar tolerance curve was flat (68;110;128;60). Therapy was started as follows: practically fat free diet; pureed vegetables; fruits limited to bananas, apples and strawberries. Breads or cereals were not restricted. Folic acid, Folvite, (15 mg.) was given daily, after demonstrating free HCl in the stomach; Vitamin B was given daily, at first intramuscularly, and then by mouth as tolerated. Alternately, he did well and poorly until 1953, at which time he was placed on a gluten poor diet (Table I). The medication remained the same with the addition of aluminum hydroxide gel (Creamalin) directly after meals for "heartburn". The results were excellent. The bulky stools disappeared, the abdomen was less protruding and not tense. He felt stronger, though weakness was evident in the evening. No longer did he have the sensation of a full rectum and he could expel flatus without fear (that it might be liquid).

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Case 2:—A white female, age 39, with a 2-year story of marked abdominal distention and bouts of diarrhea, foul stool, either bulky or liquid. About a week after she was first seen she suddenly went into tetany about 4 A.M. She had a markedly positive Chvostek's sign and there was carpopedal spasm. The serum calcium, taken on admission to the hospital, was 5.8 mg. per cent. With intravenous calcium at first, and then by mouth, together with a modified low gluten diet, she did well (since August 1953). On occasion, when she says "she just could not help it" and eats ordinary bread, she gets a distended abdomen with foul bulky stools which disappear on returning to the proper diet. One of her disturbances at present is constipation. She had a flat sugar tolerance curve, and a typical small intestinal pattern on x-ray. At present, her chemistries are normal except for the flat glucose curve. She is now on a gluten-free diet.

TABLE I

GLUTEN-POOR DIET

Breakfast:	Corn-flakes with milk, sliced bananas or strawberries. Coffee, corn muffins with butter thinly spread.
Lunch:	Tomato juice Canned salmon with tomato Corn bread with butter Coffee or tea
Dinner:	Tomato juice Broiled steak, or chicken, or any boiled or broiled meats (not fatty) Corn bread Butter Coffee or tea
Evening Snack:	Apple, banana, or applesauce.

See Table II for substitutions. New foods are to be added one at a time for at least three days before adding another new food from the lists.

Case 3:—A white female, age 40, with an 8-year history of bouts of diarrhea, "tense tummy" and a report of an x-ray typical of sprue. An attempt (less than half-hearted) to go on the modified diet was made three years ago without supervision. In August of 1955, she began to have a disturbing diarrhea. At this time her total protein was 4.68*; albumen 3.39, and globulin 1.30. By October, the total protein was 2.80; albumen 1.61 and globulin 1.19. At this time I was consulted, and she was admitted to the hospital. On admission she was quite emaciated; her abdomen was tense but not tender and she had 4 plus edema up to the mid leg (bilateral). Her weight was 95 pounds. There was no dyspnea on lying flat in bed, no distention of the neck veins and the liver was not enlarged or tender. Her blood picture showed a hemoglobin of 12.5 gm. (she had

*Protein figures are in gm. per 100 c.c. of serum. Calcium, nonprotein nitrogen, glucose, phosphorous, cholesterol, and esters are in milligrams per cent. Sodium and chlorides are in milliequivalents per liter.

been on folic acid for months), with 4.20 million red blood cells; a white cell count of 8,300, with a normal differential. The serum calcium was 7.6 mg. per cent; sodium 130.3; chlorides 100.8; glucose 78; N.P.N. 27; cholesterol 210; esters 122. She was placed on the gluten poor diet, given 500 c.c. whole blood and one unit sodium free albumen. The sodium free albumen was repeated the next day. Although the diuresis was great, it took about 8 days before the edema disappeared. Four days after admission the total protein began to rise: 3.57; albumen 2.47; globulin 1.10. On this day she started Meticorten 10 mg. t.i.d., at 6-hour intervals, to improve her appetite. (On this day, too, her stools began to harden). The Meticorten was reduced by 5 mg. every third day. No steroid was given from November 7th. She was discharged on November 12th (she begged off doing a gastrointestinal series because she felt so well).

On November 15 her total protein was 6.92; albumen 4.82, globulin 2.10, and a serum calcium of 8.2. On November 19th the diarrhea returned, the patient admitting that she had not followed the diet. The Meticorten was resumed on the 25th because the proteins were down to: total protein 5.87; albumen 4.05; globulin 1.82; calcium 7.6. At this time the prothrombin time was 44 seconds (control 12.7). In the hospital it was 17 seconds. On December 3, after complaining of stiffness in her arms, she went into tetany, requiring three 10 c.c. vials of 10 per cent calcium gluconate intravenously to relieve the spasm of the face, arms and hands. Intravenous calcium was continued for two days more and then she was placed on oral calcium, Vitamin D, and dilute HCl, as described in the discussion. On December 5, the total protein was 5.84; albumen 3.17; globulin 1.87; calcium 7.0. Prothrombin time was 26.2 seconds (control 11.0). On December 8 her feet and ankles were edematous despite a normal blood sodium. It was felt that the effervescent calcium wafers (containing sodium bicarbonate) may have been responsible for this edema, and a search for another and palatable preparation began. The lactate appeared to satisfy.

On December 12th Drisdol was given (20,000 units in 3 divided doses). Despite this, the calcium on December 19 was 7.42 (the blood phosphorous was normal on all occasions). The total protein was 6.62; albumen 4.41; globulin 2.21. On December 21, the diarrhea started again (no steroid was taken after December 2). The patient began to experiment with her own additions to the diet with dire results. Although the calcium was up to 8.4, on December 27 the total protein continued to decline to 6.28; albumen 4.41; globulin 2.21; sodium 138 m.e.q.; prothrombin time 56 seconds (control 12.3 seconds). The prothrombin time was corrected within one week with Vitamin K (hykinone) 10 mg. 3 times a week intramuscularly. On January 3, 1956, the prothrombin time was 12.3 seconds (control 11.5); calcium 7.7; total protein 5.71; globulin 1.68; phosphorus 3.7; cholesterol 368; esters 262. At this stage she was placed on a strict diet (gluten-free).

On January 19, 1956, the total protein was 6.01; albumen 4.52; globulin 1.49; calcium 7.2; sodium 145.2; chlorides 107.7; prothrombin time 13.6; (control 12.1). (Meticorten 5 mg. 4 times daily, was started on January 3.)

On February 2, the total protein was 7.81; albumen 4.62; globulin 2.19; phosphorous 4.4; calcium 9.6; chlorides 101.9; Na 141.9; K 4.1.

TABLE II

WHEAT AND RYE FREE DIET
You May Use the Following Foods

Beverages:	Tea, coffee, chocolate, milk, fruit juices		
Breads:	Corn pone, specially made bread and baked goods which are made without wheat or rye.		
	Suggested flours are: potato, soy beans, rice, corn meal and lima bean flour.		
Cereal:	Cornflakes without Malt	H-O Oats	Pure Rice Cereals
	Cornmeal	Hominy	Rice Chex
	Cheetos	Puffed Rice	Sugar Corn Pops
	Cream of Rice	Quaker Oats	Sugar Crinkles
Crackers, etc.:	Fritos, pop corn, potato chips, and special products.		
Desserts:	Cornstarch, rice, tapioca pudding, custard, ices, home-made ice cream, sherbert, meringues, Indian pudding, gelatin and rennet desserts. Special oatmeal or rice cookies–*made without wheat or rye.*		
Gravies and Sauces:	May be thickened with cornstarch.		
Eggs:	Prepared any method–*without wheat or rye products.*		
Meats:	All meats prepared without flour or crackers, etc. Instead of flour or cracker crumbs, you may use cornstarch or cornmeal or the special breads.		
Meat substitutes:	Dried beans, lentils, cheese, nuts, peanut-butter. Eggs, cornstarch may be used for cream sauces.		
Butter or Margarine:	May be used freely.		
Fats and Oil:	All fats and oil–*except wheat germ oil,* French dressing and true mayonnaise–*without wheat for thickening.*		
Fruits:	May be used freely–raw, cooked, canned or frozen *except when prepared with wheat or rye products.*		
Vegetables:	May be used freely–*except when prepared with wheat or rye products.*		
Soups:	Clear broth or bouillion or other home made soup *without wheat or rye products.* Suggestions for ingredients for soup: Rice, potato, vegetables. For home made cream soup use cornstarch for thickening.		
Sweets and Sugar:	All sugars, maple syrup, honey, molasses and syrups, jelly, jam, marmalade, candies *if not made with wheat or rye products.*		
	Check All Labels!		

Finally, it may be added that there was an amenorrhea since the outset of the present difficulty in October 1955. Gynecological examination was reported as negative.

Case 4:–This patient is included because of the favorable response to the gluten-poor diet. A 38-year old, white male, referred by a psychiatrist, gave a

history of regional ileitis with surgery two years earlier. He had a foul diarrhea with bulky stools when they were not liquid. He was much improved on the gluten-poor diet started in 1953, folic acid and Vitamin B, but the nature of his work (salesman) required him to entertain prospective buyers and he found it difficult to maintain the diet as strictly as necessary.

Comment

In reviewing the histories of these patients, in light of the combined information, the following may be added: One of the early symptoms was the voiding of a large quantity of pale urine on arising—as high as 1,000 c.c. of a low specific gravity, with no other abnormal findings. The urine the rest of the day was normal.

The nervous system was involved when the blood calcium was apparently low i.e. below 9 mg. per cent. Irritability, slight muscular twitchings, diminished muscular power (inability to do sustained work). Objectively, a faint Chvostek's sign may be the forerunner to more serious events. Finally, a continuous spasm of the muscles of the hands and feet and even the face ushers in a more serious situation calling for intravenous injections of calcium gluconate (10 per cent) which may have to be repeated two or more times before release of the spasm is brought about. Such patients must be cautioned about adhering to the diet in addition to taking calcium by mouth along with Vitamin D. The preparation used depends on the patient,—some will not be able to tolerate the chloride (10 gm. a day in divided doses) or the gluconate (15 gm.) in which instance the effervescent wafers would be given if no edema is present. Since calcium is absorbed better in an acid medium, 10 to 15 drops of dilute HCl may be given with the calcium. If necessary, Vitamin D (Drisdol), 15 to 30 thousand units daily in divided doses, may be given not only when muscular twitchings occur but also in the presence of osteoporosis. The first patient had osteoporosis of the jaw and lost seven teeth (before the diagnosis was made).

The skin was involved in that the hands were practically always chapped in cold weather and mildly so in warmer weather. Camphor ice corrected the chapping.

Only Case 2 had some anemia (9.5 gm. of hemoglobin). The red cells were hypochromic. Control of the diet was enough to correct the anemia. The use of folic acid on an empirical basis may perhaps be discontinued in the near future (on a gluten-free diet). All three patients with sprue syndrome had flat sugar tolerance curves (oral). Perhaps the use of tagged glucose may give information as to what happens to the ingested glucose.

Each of the first three patients showed an increase in the beta globulin on electrophoretic studies. Electrophoretic studies of the hemoglobin were normal.

The cases described above represent patients in whom gluten acted as an irritant to their gastrointestinal tracts. The failure to absorb fats, Vitamin K, calcium, sugar and even proteins, are all corrected by simply slowing down the intestinal motility. This can be done by diminishing the intake of gluten or eliminating it if necessary with or without the aid of steroids. The true cases of sprue represent folic acid difficulty, and since sprue cases are spectacularly improved by folic acid without any other form of treatment, the condition exemplified by our cases resemble sprue, in that long-term folic acid deficiency produces chronic inflammatory changes of the gastrointestinal tract that gives

TABLE III

WHEAT AND RYE FREE DIET–SUGGESTED MEAL PLAN
Check Lists to Be Certain About the Foods Allowed

Breakfast:	Citrus fruit or juice or tomato juice. Cereal–*not made with wheat or rye*–with milk and sugar or griddle cakes or waffles–*without wheat or rye.* Eggs Bacon, ham–if desired Bread, toast, crackers or muffins–*made without wheat or rye* Butter or margarine Jelly, jam, honey–if desired Coffee, tea or milk
Luncheon:	Special soups–if desired Cheese, eggs, meat (no cold cuts), fish or peanut-butter, Bread–*Not made with wheat or rye* Butter or margarine Vegetable or salad or both Milk, tea or coffee Fruit, custard, gelatin dessert, pudding (see list) special baked products
Supper:	Fruit or fruit juice or special soup–if desired Meat, fish, fowl or liver White or sweet potato or rice Vegetables Butter or margarine Bread or other products *not made with wheat or rye* Jelly, jam, etc.–if desired Milk, tea, coffee, soda or fruit juice–as desired Fruit or other dessert from allowed list
Between Meal Suggestions:	Fruit, fruit juice, candy, carbonated beverages, Fritos, cheese, special baked products or other items on allowed list.

an x-ray pattern similar to sprue. All other symptoms are attributable to the diarrhea and faulty absorption. We have, therefore, in our cases a disease or syndrome characterized by sensitivity of the gastrointestinal tract to gluten as a result of which there is a loss of essential carbohydrate, protein and fat, along with minerals (calcium) and vitamins (K; folic acid) and, in 3 cases similar electrophoretic patterns. The loss of these brings on a chain of symptoms such as are embodied in the cases described above. The characteristic odor of the bulky or liquid stools (due to decomposition of gluten), (examination of stool reveals increase in neutral fat or fatty acid); the gaunt face; the thin

arms and legs; the protruding abdomen—all of these, along with the chemical changes and vitamin deficiencies, form a chain of symptoms which should lead one to try the therapeutic tests of using a gluten-*free* diet. When that is determined, then the gradual addition of gluten-poor foods could be tried, one at a time. Steroid therapy should be used only when urgently necessary.

One must keep in mind that simply telling the patient to avoid gluten or malt-containing food is not sufficient. Before a decision is made that gluten or malt is not involved in a particular case make certain that the patient knows enough to *read* all labels. Simple inquiry from a person who sells food may not be the wise thing to do.

Even in mild cases there should be no difficulty in calcium or Vitamin K absorption. The more severe cases require a strict gluten-free regimen, with perhaps the addition of steroid therapy when urgent or when the appetite is poor. It may be stated here that the four patients described above represent a single type of personality. They are rather quiet people who perhaps resent being told what to do, and not following the doctor's orders is a form of rebellion. The body types are similar to that seen in celiac disease—everything skinny but the "pot belly" (which is skinny too, but distended). On first seeing such a patient—a history of large bulky stools, foul diarrhea (either multiple solid or semi-solid, or liquid stools), a flat oral sugar tolerance curve and a typical small bowel x-ray pattern, gluten sensitivity should be entertained as a possible cause. Proper discussion with the patient on the likely course of events may bring cooperation. A test diet is given. Case 1 (loss of 40 pounds); Case 2 (tetany); and Case 5 [severe enough diarrhea to require (?) surgery] have been and are doing well on this diet. True, it is limited, so that the addition of fats other than olive oil, or bulky foods, such as leafy vegetables, etc., will bring a more moist stool, if not diarrhea. If a patient does not respond to this diet, a strict gluten-free diet should be given. Finally, steroids may be given to stimulate the appetite or to try to terminate a persistent diarrhea. The good results obtained with steroids should not cloud the possibility of a gastrointestinal lesion.

That gluten is responsible for the odor may be demonstrated by the return of the characteristic odor of the stools within several days after ingesting foods containing gluten, and its disappearance in 2 to 3 days after stopping. Chemically, on separating, the wheaten flour contains 70 per cent starch and 10 per cent of a sticky nitrogenous substance called gluten. When moist this gluten soon decomposes and smells disagreeably.

It is advisable to add one food at a time when expanding the diet, in order to study the effects for 2-3 days. When steroid is to be used, 10 mg. Meticorten every 6 hours around the clock may be given until the desired results are obtained and then the Meticorten may be reduced by 5 mg. doses

every second day. Whether or not the Meticorten is to be given in maintenance doses over a period of time depends on symptoms, weight, and blood chemistries.

The onset of tetany may be explained in the same way as in other malnutrition. With lack of absorption, the minerals are withdrawn from bone to maintain blood figures. Osteoporosis may be seen on x-ray. The blood phosphorous was normal in both patients with tetany. That tetany occurred in Case

TABLE IV

WHEAT AND RYE FREE DIET
Do Not Use the Following Foods

Beverages:	Malted milk, Postum, Mellins food, Nestle's food, Cocomalt, Ovaltine. Instant coffee (if it contains cereal products) malt, gin, beer, whiskey.		
Bread:	All breads made with wheat and rye, hot breads and muffins, regular oatmeal bread, corn bread, baking powder biscuits, Zwiebach, pretzels, gluten bread, Rye-Krisp and other rye wafers.		
Cereals:	All Bran	Krumbles	Ralston Superfine
	Beemax	Mellowheat	Rice Krispies
	Bran Flakes	Muffets	Shredded Ralston
	Cheerios	New Oats	Shredded Wheat
	Cornflakes	Pablum	Wheat Chex
	with malt	Pep	Wheat Flakes
	Crackels	Pettijohn	Wheat Germ
	Cream of Wheat	Post Toasties	Wheaties
	Farina	Puffed Wheat	Wheatworth
	Grapenuts	Ralston	Whole Bran
	Grapenuts Flakes	Kix	
Crackers:	All crackers and cookies, rusk, matzoh, *except* specially prepared items, not made with wheat or rye.		
Desserts:	Pies, cookies, cakes, doughnuts, ice cream cones, prepared mixes—*unless label proves they are made without wheat or rye.*		
Meat and Meat Products:	Meat prepared with flour, bread or crackers as croquettes, meat loaves and stew thickened with flour or made with dumplings. All commercially prepared meat products as sausages, frankfurters, cold cuts and meat loaf where wheat may be used as a filler. Gravies and sauces thickened with flour.		
Soups:	Canned broths or consomme or creamed soup with wheat products.		
Salad Dressings:	All cooked or boiled salad dressing where flour is used for thickening.		
Other Foods:	Griddle cakes, pancakes, waffles unless prepared without wheat or rye, macaroni, spaghetti, noodles, pastina, etc.		
Flours:	Wheat flour, graham flour, rye flour.		

Check All Labels!

3, with a serum calcium of 7.6 mg. per cent after her discharge from the hospital, may be explained by the fact that more calcium was bound by the higher serum protein (5.87 gm. per cent) at that time than at the time of admission, when with the same serum calcium the proteins were 2.80 per cent. The available ionized calcium was sufficient at the time of admission to prevent tetany.

Conclusion

Three patients with sprue syndrome and one with regional ileitis were presented to demonstrate sensitivity to gluten. One (Case 3) had a very low blood protein on admission to the hospital: total protein 2.80; albumen 1.61; globulin 1.19.

Since this paper was written, an associate of the writer, Dr. Louis Greenwald, asked me for a copy of my gluten-poor diet for a patient of his who had 3 operations for bleeding gastric ulcer. Following the last operation in 1955, he developed a foul diarrhea which did not respond to the usual medications.

Dr. Greenwald reports: ". . . he was placed on a gluten-poor diet, as you suggested, and within 12 hours, the first time in many months, the patient had a normal formed stool daily. . . . The patient, who is reliable, mentions that when he digresses from the diet he becomes flatulent and his stools become loose".

The author wishes to thank Miss Virginia Rechnitzer for her technical assistance.

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CARCINOMA OF THE DESCENDING COLON TO THE RECTOSIGMOID*

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In the treatment of carcinoma of the colon from the cecum to the right transverse colon a right hemicolectomy is the operation of choice. This procedure fulfills the criteria of a good cancer operation which aims to remove the tumor and all the resectable avenues of spread.

Because of the anatomical distribution of the blood supply from the superior and inferior mesenteric arteries and because of the lymph drainage towards the superior and inferior mesenteric group of lymph nodes and the desire to save the rectal sphincter, carcinoma of the left colon, from the midtransverse colon to the rectum inclusive, offers a more difficult problem in treatment. Many operations have been developed for carcinomas in this area, but there is no uniformity of opinion as to the best procedure to be followed.

In the planning of an operation for carcinoma of the left colon the primary objective is to effect a cure of the cancer irrespective of how radical the operation should be in order to accomplish this end. Fortunately the colon, because of its segmental blood supply and lymphatic drainage, lends itself to radical resection. Also, long segments of colon can be removed without any appreciable change in the patient's bowel function.

Preoperative Management

Preoperative preparation of a patient who is to undergo surgery for carcinoma of the colon consists essentially of restoring the patient's general condition to as near to normal as possible by a high protein, high carbohydrate and high vitamin diet, with correction of any secondary anemia by multiple blood transfusions.

The use of antibacterial agents in order to reduce the number of bacterial organisms in the colon is a well established practice. It is described elsewhere in this symposium.

Factors Determining the Choice of Operation

The choice of operation for carcinoma is determined by the site of the tumor, its local spread, and regional lymph node drainage. Clinical pathological studies of Westhues, Gilchrist, David, Duke and Waugh have established the course of lymph node spread of carcinoma of the colon and also determined the rather limited spread of carcinoma in the bowel wall, either proximally or

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distally to the tumor. As a result of these studies there has developed a generally uniform opinion among surgeons as to the amount of bowel that should be removed in order to eradicate the local spread of the malignant growth in the bowel wall itself. There is no such uniformity of opinion as to the extent of lymph node resection necessary in order to effect the greatest number of cures. It may be that the disparity in the percentage of cures obtained for five or more years is due to variations in the extent of resection of the potentially involved regional lymph nodes as practiced by different surgeons. A disparity is also found in the results obtained in carcinomas of the various segments of the colon.

The percentage of five-year survivals in our series of 385 cases of carcinomas of the colon operated upon from 1940 to 1950 was higher when the disease was present on the right than on the left side. Since the type of the tumor and method of spread are essentially alike in all segments of the colon, it was felt that the limited extent of resection of the potentially involved lymph nodes was probably the cause of the fewer cures of carcinomas in the left colon. In order to improve our results, particularly in cancer on the left side, we have extended our resection of the colon and mesocolon so as to include the greatest number of lymph nodes that drain the involved segment of bowel.

Descending Colon to Rectosigmoid:—Tumors of the descending and sigmoid colon to rectosigmoid, have a definite pattern of upward spread from the regional lymph nodes around the inferior mesenteric artery and aorta.

In a study of 36 patients with carcinomas of the left colon in which lymph node spread was determined by formalin-fixed, surgically resected specimens, three patients, or 8 per cent, had involved nodes along the inferior mesenteric artery from its origin at the aorta to its bifurcation; or approximately within 1 cm. of the aorta. Five patients, or 14 per cent, had carcinomatous nodes within 2 cm. of the aorta, and eight patients, or 22 per cent, had malignant cells in lymph nodes within 3 cm. from the aorta. The operation of choice for carcinomas of the descending and sigmoid colon up to the rectosigmoid is a resection of the left colon with its entire lymph node containing mesentery from the splenic flexure to the rectum, that is, a left hemicolectomy. The continuity of the bowel is reestablished by an anastomosis of the colon from the region of the splenic flexure to the rectum. The postoperative morbidity and mortality in our series was essentially the same following limited segmental resection of the colon as following a left hemicolectomy.

Rectosigmoid:—Tumors in the region of the rectosigmoid, as shown by histological studies of resected specimens, spread predominantly upward along the inferior mesenteric group of lymph nodes with little tendency to spread retrograde below the lower edge of the tumor. Carcinomatous involved lymph nodes are rarely found more than 4 cm. below the lower border of the tumor,

although isolated instances are recorded in which metastatic carcinoma was found in lymph nodes that lay 10 to 15 cm. below the tumor. The results of these histological studies of resected specimens have been accepted by surgeons as guides in determining the length of colon to be resected proximally and distally to the carcinoma. Very little attention has been drawn to the fact that these studies were done on formalin-fixed specimens which may have contracted considerably as a result of the action of the fixative.

In the transference of distances obtained from the study of formalin-fixed specimens back to the living patient, allowances must be made for the amount of contraction of the bowel after it has been resected, which is often as much as 50 per cent, and for further retraction if the bowel is fixed in formalin without first being pinned to a board so as to maintain its original size. Since the length of the resected bowel is rarely measured first in its living state in the patient and then in its fixed state in order to obtain the factor of contraction, the distances obtained in histological studies of resected specimens of the colon are only approximate; they may often be only one-half to one-third the actual distances in the respective patients. If histological distances are interpreted with the knowledge of the contraction factor for the specimen they can be reliably applied in clinical surgery. If the histological distances are interpreted without the knowledge of the specimen contraction, they cannot be applied to the patient without first empirically assuming the contraction factor of two or three. If, for example, the carcinomatous node is found 4 cm. below the tumor in an unpinned formalin-fixed specimen, in the patient this distance would probably have been about 8 to 12 cm. below the tumor.

The high incidence of local recurrence following segmental resections of carcinoma of the rectosigmoid, notwithstanding the limited retrograde spread perceived in resected specimens, is in all probability due in part to the direct application of uncorrected histological distances to the patient with the result that local, probably resectable carcinomatous tissue is left in the patient. Such underestimating of the extent of retrograde spread of the carcinoma may also cause carcinomatous lymph nodes to be divided and the malignant cells to be seeded locally. Because of these two potential dangers it has been our practice never to attempt a segmental resection of the rectosigmoid unless from 12 to 15 cm. of bowel with its mesentery below the tumor can be removed.

Upward spread of carcinoma of the rectosigmoid is towards the inferior mesenteric group of lymph nodes. The operation of choice for carcinoma of the rectosigmoid is a resection of the tumor and all its lymph node spread up to and including the inferior mesenteric and periaortic lymph nodes that lie along the origin of the inferior mesenteric artery and resection of the bowel and mesentery to about 12 to 15 cm. below the lower border of the tumor. The continuity of the bowel is then reestablished by an anastomosis between the colon in the region of the splenic flexure to the rectum.

In those patients in whom it is not possible to remove 12 to 15 cm. of bowel and mesentery below the lower border of the tumor, an abdominoperineal resection with left hemicolectomy is done.

Rectum:—Carcinoma of the rectum, because of its location in the midst of the rich lymphatic network in the pelvis, spreads upward along the superior hemorrhoidal to the inferior mesenteric and periaortic nodes but also spreads laterally along the middle hemorrhoidal, hypogastric and iliac group of lymph nodes. Because of this wide local dissemination of carcinoma of the rectum, complete eradication of the tumor tissue is difficult. The operation should be planned so as to remove all the regions of local infiltration and metastases. The operation of choice is an abdominoperineal resection with a resection of the mesentery of the left colon up to the origin of the inferior mesenteric artery, which is divided at the aorta, and dissection of the periaortic lymph nodes. The colon in the region of the splenic flexure is brought out as a colostomy through a stab wound in the left upper quadrant. Since metastatic carcinoma is found in lymph nodes along the middle hemorrhoidal, obturator, hypogastric and iliac chain of lymph nodes in as high as 24 per cent of the advanced carcinomas of the rectum, abdominopelvic node dissection should be performed more frequently than it has heretofore in the hope of increasing the curability of this group of tumors.

Carcinoma of the rectum which has extended into the pelvic urogenital system presents particular problems. In females, in whom there is infiltration of the posterior vaginal wall or uterus by rectal carcinoma, resection of the genital tract, that is, ovaries, tubes, uterus and vagina, along with the attached tumor is necessary in order to give the greatest chance of a cure. In males, extension of rectal cancer into the urinary bladder may require local resection of the bladder. Infiltration of the seminal vesicles and prostate may require excision of these organs if the extension seems to be limited to them. If, however, tumor tissue has extended beyond these structures, complete removal of the pelvic viscera with implantation of the ureters into the bowel or skin gives the patient his only hope for the relief of his symptoms or a possible cure.

Palliative colostomy, except for the relief of symptoms of bowel obstruction, offers little or no relief from the ravages of the infiltrating carcinoma.

Acute intestinal obstruction secondary to stenosing carcinoma of the colon is a complication that must be remedied before definitive surgery for the carcinoma can be performed. Primary resection of the tumor in the presence of an intestinal obstruction is associated with a much higher mortality than resection of the carcinoma in the absence of obstruction. The obstruction of the colon should always be relieved before definitive surgery for the carcinoma is undertaken. This subject is discussed in a separate paper.

X-RAY LESIONS OF THE SMALL BOWEL*

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It shall be the purpose of this presentation to briefly reiterate some of the landmarks in the development of present day methods of study of the small intestine, and to direct attention to some of the changes which the x-ray alone will reveal. In addition, three types of conditions in which x-ray study has proven very helpful will be presented.

During the past 35 years much attention has been devoted to the study of the gastrointestinal tract. Only a minor part of the time and effort has been spent on this most important sector of the digestive system, if one excludes the duodenum and the terminal 15 inches or so of the ileum. There has been justifiable reason for this state of affairs because of the time consumed and the inability of this portion of the bowel to lend itself to study in routine fashion. Walter Mills, in 1922, was one of the first to become interested in the study of the small intestine. He emphasized in an article, in those early days, that organic lesions in the small bowel might be demonstrated as in the stomach or colon if the loops of bowel could be clearly seen[1]. In the decade preceding this, Haudek and Akerlund had made important observations relative to the anatomic basis for diagnosis of duodenal ulcer, and the use of fluoroscopic screen control of compression technic in the roentgen examination of the duodenum[2]. Pasquera was one of the first to resort to intestinal intubation by which method he introduced barium into the small bowel. A good account of this method was given later by Shatski in 1943[3]. The use of the Miller-Abbott tube is familiar to all of you and has been utilized in introduction of the opaque meal for localization of lesions in the small intestine. Mackie and Snell and Camp were among the first observers to point out certain roentgenologic changes frequently seen in those patients suffering with sprue or idiopathic steatorrhea.

The overlapping intestinal loops present many difficulties to the gastroenterologist. Fortunately the duodenum and lower portion of the terminal ileum are much more easily demonstrated than the midportions of the small intestine. In spite of the confusion, there are orderly landmarks which are most helpful in recognizing the various sections of the small intestine. Familiarity with the "C" or horseshoe curve of the duodenum in the right midline as it extends over to duodenal jejunal flexure is in most cases easily demonstrated. The jejunum is recognized radiologically by Kerkring's folds or the *valvulae conniventes*. It is normally located in the left side of the abdomen. The jejunum joins the ileum in the midlower abdomen and folds are directed toward the right side.

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There are essentially six groups of coils, namely: duodenal, duodenal jejunal flexure and upper jejunum, midjejunal loops to the left lumbar area, lower jejunal and upper ileum in the left lower quadrant, the right ileal loops in the midline and in the right lumbar area, and the lower ileal loops in the right lower quadrant. This division serves well in recognizing which section of small intestine one might be viewing. Particular attention must be paid to the appearance of the mucosal pattern as it is typically feathery in the jejunum and as one approaches the ileum the markings become less prominent; at times not visible. The caliber of the bowel likewise becomes smaller as one approaches the ileum. In my experience the mucosal pattern has been a more reliable landmark than has the caliber of the bowel for the reason that the latter is constantly changing and is subject to tension. I am of the opinion that this matter of tension is reflected throughout the entire intestinal tract and that in instances of colon spasm you frequently find motility is retarded in the small intestine and the loops appear larger than normal. This factor may be responsible for clinical situations which we frequently see where patients complain of indigestion, fullness with small amounts of food, etc., and there is no perceptible evidence of organic disease in the stomach, gallbaldder, or small intestine. As soon as the spasm has been relieved, there is almost automatic relief from the symptoms referable to the upper gastrointestinal tract.

In addition to recognition of the anatomical landmarks one must constantly be mindful of the motion of the bowel. The movements are best divided into pendulum, segmental, peristalic or forward movements, and divisional. As viewed under the fluoroscope the barium column is usually seen as a continuous stream with an occasional empty segment due to peristalic contraction. These contractions in the duodenum and jejunum are of great moment as compared with the lesser, shorter peristalic waves characteristic in the ileum. Transit time depends upon this type of activity in the small intestine and it becomes obvious therefore that any lesion which is to be detected must have some effect on motility, change in mucosal pattern, produce some degree of obstruction or grossly change the anatomical pattern of the small intestine. Obstructive lesions do not need to be intrinsic within the bowel itself, but may arise in some contiguous organ. This fact emphasizes the necessity for careful examination, inasmuch as certain regions of the abdomen may harbor a disease process which might be recognized from its influence on distortion of the small intestinal pattern. Tumors of the mesentery and adhesive bands fall in this category and can under certain circumstances be suspected from their effects in this way.

The methods used in detecting lesions of the small bowel are of several varieties and are subject to limitations. The plain flat film of the abdomen I feel should be constantly used as a starting point in order that any gas pattern might be detected and any radio-opaque matter visualized before barium is to be introduced. Should any gas be noted in the small intestine, various films

should be made in the lateral position, both standing and supine, and in the A. P. with the patient lying on both the right and left side. Immediately after the flat films have been exposed and are satisfactory, the patient may be given a barium meal consisting of two ounces of barium to four ounces of warm water. The amount of the mixture administered depends on the size of the patient. It is a general rule that smaller amounts of barium meal are more easily followed through the small intestine. Frequently larger amounts are administered in an attempt to completely fill the stomach. This factor at times interferes with proper study of the loops of small bowel. In the beginning the barium will be seen to pass from stomach into the duodenum where visualization of this portion of the small bowel can be made out satisfactorily. As it leaves the duodenum and starts into the jejunum and ileum, the frequency of fluoroscopic observations depends entirely upon the patient being studied. Some prefer fluoroscopy and radiography at certain time intervals, while others choose to individualize examination and watch carefully as the barium progresses, taking films at appropriate intervals to record certain sections which might be of suspicious character. It is obvious that careful study will follow no routine, and consequently where routine examination has been the rule and practice, lesions which might easily have been demonstrated have been missed.

It is the aim of the gastroenterologist to visualize the contour, distensibility, mucosal pattern and mobility of every loop when possible[4]. When certain loops cannot be distinguished a small intestinal enema may be resorted to, or in some cases the barium-saline ice water technic of Weintraub and Williams may be used. Various ways of compressing the bowel have been utilized so that particular areas might be better seen. I have found the compression paddle to be of invaluable service in this regard. Fluoroscopic and radiographic advantage has come from tilting the table at various degrees. It might be stated that unless the tilt is acute at least at an angle of 60 or 80 degrees, little will be gained. In certain instances it has been found advantageous to give the patient several glasses of water to drink in order to distend the bladder before the examination proceeds. This will tend to lift some of the loops of the intestine upward from the pelvis. Water enemas, in order to distend the colon have served similar purposes in showing better certain obscure loops of the small bowel. No single technic or combination of technics has proven one hundred per cent effective in demonstrating certain lesions. One of the disconcerting factors is that in some instances constant defects may be most obvious and at operation no lesion can be discovered. On the contrary, there have been careful studies made on the small intestine which were not revealing of any pathological process and at operation regional ileitis has been found. Regardless of the technic used, one cannot feel that a thorough investigation has been made of the small intestine until a concerted effort has been put forth in the direction of visualization of each and every loop. I feel that this has been satisfactorily accomplished if careful fluoroscopic observation and serial films are made of certain areas which may not be well defined fluoroscopically and of which a more

permanent record is taken on the x-ray film. As it has been previously mentioned, the compression paddle has served nobly during the course of these examinations.

A great variety of pathological lesions have been discovered by roentgen examination of the small intestine. Enumerated in Table I are some of these various conditions. I realize that this is in no way complete, however, it serves to demonstrate not only the great many things which may present themselves, but also the rarity with which they occur. Duodenal ulcer is conspicuous by

TABLE I

STATISTICAL OCCURRENCE OF SMALL INTESTINAL LESIONS

Enterogenous cysts	Rare
Nonrotation of intestine	Rare
Meckel's diverticulum	.02 per cent population
Diverticulum jejunum	Very rare
Diverticulum duodenum	Occasional
T.B. jejunum	Rare
Benign tumors 50 per cent ileum	Rare
Polypoid tumors	Rare
Lipoma	Rare
Myoma	Rare
Fibroma (Rarest type tumor of s.i.)	Very rare
Hemangioma	Rare
Neuroblastoma	Rare
Carcinoid	Rare
Pneumotosis	Rare
Enteritis	Fairly common
Regional ileitis (jejunum 3.5 per cent cases)	Occasional
Cancer (.05 per cent necropsy) (3 per cent are intestinal ca.)	Uncommon
Sarcoma (Lymph structure involvement)	Rare (.05 per cent)
Syphillis	Very rare
Enteroliths (.2 per cent of obstruction)	
Intussusception (.002 per cent children .02 per cent)	Rare
Mesenteric occlusion .001 per cent	Rare
Adynamic ileus (postoperative)	Uncommon
Spastic ileus	Very uncommon

its absence from this list for the reason that it is probably the most common lesion in the small intestine and does not present the diagnostic problem that these other lesions might. It should be noted that diverticulum of the duodenum and regional ileitis are found with more frequency than most of the other lesions listed. Attention is directed to the rarity of various lesions in the small bowel. With this in mind, I should like to call attention to three types of conditions which not uncommonly alter the small intestinal pattern. The first

of these is gastrointestinal allergy which can at times be very successfully demonstrated by administration of the suspected allergen in the barium meal and observing the marked changes which may occur in the small intestinal pattern. It can be seen from the films (Fig. 2) gastric motility is delayed when the allergen is administered. There is marked irritability and segmental spasm throughout the proximal ileum and there is a delay in motility throughout the small intestine. A second type of condition arises in those patients who harbor intraabdominal adhesions, usually as a postoperative complication. It is not infrequent that the gastroenterologist is called on to diagnose those cases with partial obstruction due to postoperative adhesions in whom cramping pain, nausea and vomiting, and at times diarrhea are present. Perseverance in demonstrating individual loops will be rewarded by the finding of changes in the

Fig. 1

Fig. 2

small bowel which direct suspicion upon a particular segment which is giving rise to symptoms. This can at times be confirmed later at operation. A third condition of interest which I am sure occurs with much greater frequency than one might be superficially led to believe includes those persons with neurogenic diarrhea and emotional upsets which seem directly reflected into the gastrointestinal tract. In such instances as these almost any variety of x-ray patterns may be exhibited and motility may be a very variable and changing factor. Such cases frequently are puzzling for they present similar findings to those encountered in gastrointestinal allergy although inclusion of the allergen in the barium meal at a later time is in most instances decisive. Where the conditions co-exist the proper diagnosis is extremely difficult. L. S. Goin in 1952 emphasized the effects of emotional states on the small bowel as well as some

of the bizarre findings associated with intestinal allergy[5]. Fortunately there are other methods of arriving at a diagnosis of emotional states and intestinal allergy. It is important, however, that the gastroenterologist must be cognizant of the fact that these conditions may reflect themselves in the small intestinal pattern. Where motility may be markedly upset small intestinal study may be particularly informing inasmuch as the colon may not be overwhelmed by the rush of the intestinal content into the large bowel and consequently no clinical diarrhea manifested. Recognizing of course that diarrhea does not exist unless there has been frequent passage of watery stools from the rectum. The following case histories are presented to demonstrate the three varieties of cases before mentioned:

Case 1:—Mrs. E. W., age 53, complained of attacks of abdominal cramping pains lasting two to ten hours during the past eight years. These attacks were

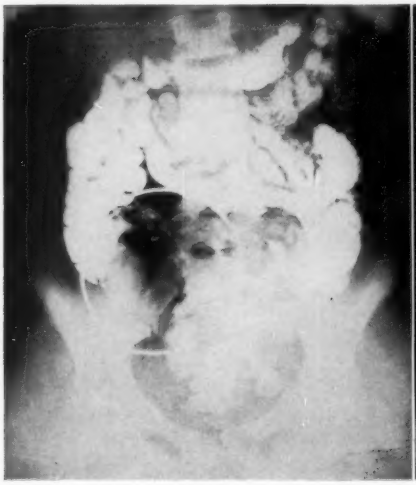

Fig. 3

Fig. 4

associated with spells of rhinorrhea, wheezing and cough. She likewise became constipated during these attacks. She had observed that eggs and raw salad were apt to precipitate these symptoms. Her gallbladder had been removed, soon after the symptoms presented themselves about eight years before. An initial blood count was done and the white count was 10,600. A gastrointestinal study was done and the findings in the small intestine were as shown in Figure 1. The examination was repeated about a week later under about the same conditions with the addition of a raw egg to the barium mixture. In Figure 2 you see the marked changes in the small intestinal pattern which have been provoked by the allergen. The patient was followed for about two years and had no recurrence of symptoms and was free from the upper respiratory symp-

toms as well. This patient had had skin tests done about a year previously with no conclusive findings at that time.

Case 2:–Miss B. K., age 19, chief complaint was intermittent attacks of diarrhea during two and one-half years, cramps in the abdomen and mucus in the stool were noted from time to time. There had been a loss of weight during the past three to four months before examination. The onset of symptoms had been gradual with periods as long as 30 days asymptomatic. During the six months previous to seeking help the patient had noted four to six stools daily. Proctoscopic examination was done with the examination of stools for occult blood, parasites and there was on several occasions positive occult blood in

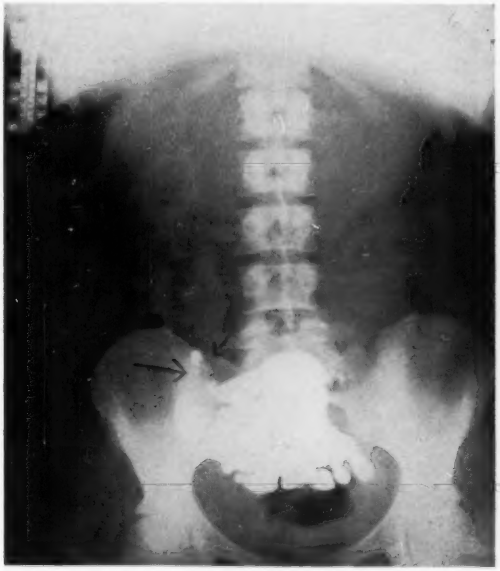

Fig. 5

the stool. Mucus was likewise found on several occasions. Gastrointestinal study was done and as you see in Figures 3 and 4, there is hypermotility throughout the small intestine with segmental spasm and irritability a prominent feature. The terminal ileum was suspected of being abnormal and about a month later examination was repeated. Again the bizarre pattern seen in the ileum was presented. Examination was repeated three or four times, and it was finally felt advisable to resort to surgical exploration so that if the patient was harboring any regional ileitis it might be corrected before the process became too extensive. At operation the surgeon was unable to find any abnormal situation within the abdominal cavity. The interesting thing about this case was that

the mother, about a week after the operation, volunteered the information that the father had had the same sort of symptoms for the first several years of their courtship and after marriage was completely free of symptoms. Since the patient has been reassured, she is much improved.

Case 3:—Mrs. M. H., age 25. The chief complaint was nausea and vomiting and cramping abdominal pain with attacks of distention of the abdomen. A loss of weight of 30 pounds, loss of appetite and diarrhea were present for about four months. The patient gave a history of two caesarean operations with a hysterectomy one year before her first visit to the office. She stated she was unable to keep water down at times and that the symptoms had no relation to meals. The cramping pains were present almost constantly in the lower

Fig. 6

Fig. 7

abdomen. There had been no bloody stools. Gastrointestinal examination was done with the findings as seen in Figure 5. The x-ray findings suggest an obstructing type of lesion about four to five inches from the ileocecal valve with a marked narrowing of the terminal ileal loops, It was also suggested that the cecum might be involved in the process. About two weeks later the patient was hospitalized and exploratory laporatomy was done, at which time string-like adhesive band, running from the distal ileum about five inches above the ileocecal valve to the anterior abdominal wall and also communicating with the ascending colon at a point five or six inches above the cecum was demonstrated. This produced a hiatus through which the more proximal ileum was herniating. The adhesion was severed by the surgeon and the abdomen was closed. There was no evidence at the time of operation of a regional entero-

colitis or other pathology. The patient has been followed for five or six years and has had no symptoms.

Case 4:—Miss V. E., age 44, first seen April, 1954, at which time she complained of chronic urticaria for two years. Her past history was negative for any allergic symptoms. She had been operated upon on two occasions for intestinal obstruction. The reason for this was not clear. Two or three months after the second operation, the symptoms of urticaria and chronic constipation started. Because of the constipation the dermatologist sought my consultation. I was told that after enemas and laxatives, which managed to cleanse the bowel, she was somewhat relieved from the hives for 24 to 36 hours. With this in mind a gastrointestinal examination was done with the findings as are seen in Figures 6 and 7. It was concluded that intraabdominal adhesions must be responsible for the bizarre small intestinal pattern. An exploratory laporatomy was done about a week later, and the surgeon described multiple whitish nodules about the size of a pin point studded over the midportion of the ileum. The ileum, about 20 inches above the ileocolic valve, was matted together in a fist size mass and it was evident that proximal loops were distended due to obstruction in this area. The surgeon felt it best to remove the kinked loops en bloc and about 20 inches of proximal ileum were removed. Continuity was restored by primary end-to-end anastomosis. Pathological examination of specimen and the nodules which the surgeon had noticed came from talcum powder which had been used on the gloves at previous operation. Immediately after operation the patient's hives began to clear up and, although not entirely free, she was very much relieved from her distressing symptoms.

Conclusions

The small intestinal tract does not lend itself to routine examination and becomes an individualized study.

Functional derangement, allergic factors, postoperative adhesions probably account for changes in the small intestinal pattern more frequently than is usually anticipated.

Careful small intestinal study may reveal, or at least point to pathological processes in contiguous organs.

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COLONIC DIVERTICULITIS

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Bloomfield, N. J.

Differential Diagnosis and Medical Management

When sacular protrusions of the colonic wall are complicated by inflammation, we have a condition known as diverticulitis. It has been established that five to ten per cent of persons over the age of 40 have diverticulosis and that 17 to 27 per cent of these patients have diverticulitis at some time in their lives. The complications of diverticulitis occur in 20 to 25 per cent of these cases, giving us an estimated 1 in 500 patients (Table I).

In Figure 1, we see the age distribution as it occurred in 72 cases of diverticulosis[1]. Thirty-seven per cent of the people past the age of 50 will have diverticulosis.

The diagnosis is best made by: 1. X-ray; 2. Symptoms; 3. Laboratory tests, and 4. Sigmoidoscopic examination.

TABLE I

5-10 per cent of persons over 40 have diverticulosis

17-27 per cent have diverticulitis at some time

20-25 per cent of these cases have complications of diverticulitis

1 in 500 patients with diverticulosis will have complcations

Symptoms

Simple acute diverticulitis may involve any portion of the colon, but is more common in the sigmoid. It is frequently referred to as "left-sided appendicitis" because of the resemblance to the signs and symptoms of acute appendicitis. Pain is usually in the left iliac fossa, which may be cramp-like or dull. The pain may radiate to the left side and to the back. In women the pain will become more severe with the menstrual period. If diarrhea is present, the pain is usually more severe with each bowel movement and subsiding between them. Tenderness and rigidity are associated with the local pain. Nausea and vomiting are not uncommon.

Temperature, more like the septic type, may be present. The symptoms may subside in one or two days following resolution of the process, or they may continue on with complications. The symptoms of diverticulitis will depend on the degree of inflammation and the nature of any complications. Brown and Marsley[2] concluded that in one-third of the cases of diverticulitis, symptoms are the result of inflammation and in two-thirds the result of obstruction plus inflammation.

Laboratory Tests:—The white cell count may be elevated and the sedimentation rate is usually elevated.

Figure 2a is an x-ray of a female 64 years of age. This patient was first seen by me in 1948, at which time she was having persistent diarrhea with eight to nine bowel movements per day. There was vague left lower quadrant abdominal pain. She had blood in the stools but no ova or parasites were found. A sigmoidoscopic examination up to 18 cm. was negative.

Barium Enema:—Diagnosis, diverticulitis with abscess and obstruction was made. There was a temperature rise, secondary anemia with a normal white cell count, and an increase in the sedimentation rate. Weight was 132 pounds. She was slightly tender in the left lower quadrant.

Course:—She was placed on a low-residue diet, given antispasmodics, mineral oil and Thalamyd. She also received supportive therapy. For one year

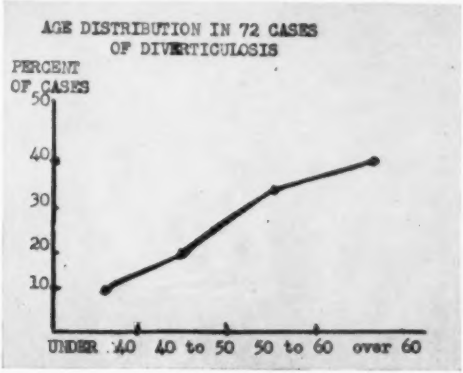

Fig. 1

she had frequent attacks of pain with some loss of weight of about ten pounds. The diarrhea was controlled with Kaopectate and bismuth subnitrate. After one year of strict diet and supportive treatment she began to gain weight, had normal stools and today weighs 155 pounds. She continues to take one Thalamyd, twice a day; Trasentine, one before meals, and occasionally will take bismuth for gas. She still avoids roughage. This case could have been operated on and complications, such as fistulae might have resulted. The persistent medical care has restored her to health.

Figure 2b shows the evacuation film. She has recently been x-rayed by me and shows no obstruction or diverticulitis at present.

Sigmoidoscopic Examination

Using the regulation sigmoidoscope, the examiner usually fails to see the presence of diverticula. Willard and Bockus[3] have seen only one diverticulum

through the scope in ten years. This examination is of value in differential diagnosis. One must be sure we do not have polyps or carcinoma complicating the diverticulitis.

The complications of diverticulitis are: 1. Localized abscess; 2. perforation and peritonitis; 3. fistula and 4. mechanical obstruction.

Differential Diagnosis

About two-thirds of the patients with carcinoma of the large bowel have a lesion which is palpable by rectal examination or can be seen with the

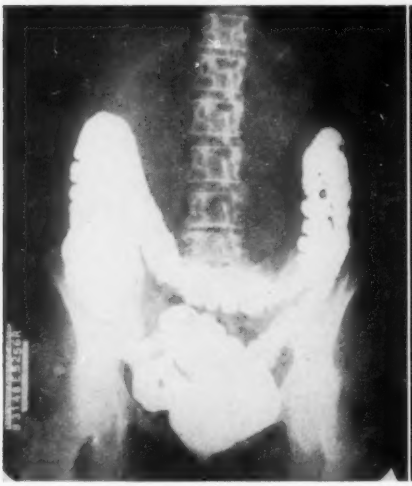

Fig. 2a

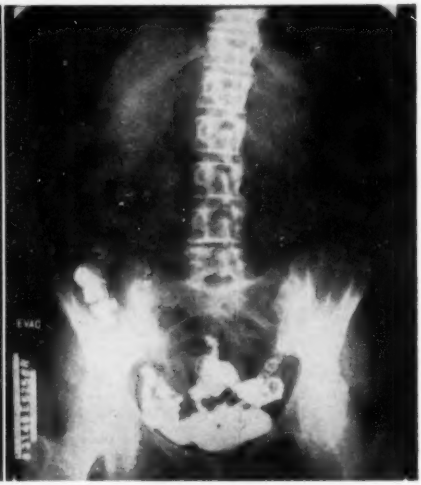

Fig. 2b

sigmoidoscope. About one-half of the remaining patients have tumors in the sigmoid area or descending colon, where diverticulitis usually develops.

Case Report

C. W., a 69-year old male, was first seen by me in October 1954, at which time he complained of gas and distress in the lower abdomen, which had started during the summer. There was no nausea or vomiting. Distress came on at any time, and there was a definite change in bowel habit. He had been avoiding roughage. The stool examination revealed a 4+ occult blood. He had been treated for the past three months for upper gastrointestinal disease and six weeks prior to my seeing him a gastrointestinal series was done and was reported as negative. His past medical history revealed that he had a duodenal ulcer three years prior to this examination. A blood count (in the office) revealed a secondary anemia and 12 mm. sedimentation rate (Cutler method)

at the end of one hour. There had been only about two pounds loss in weight. The abdomen revealed only some slight tenderness in the right lower quadrant, where no mass was palpable. Because of the above symptoms and change in bowel habit, the patient was sigmoidoscoped and nothing was found up to 18 cm.

Barium Enema:–The barium was passed through to the middescending colon where an obstruction was encountered. Numerous diverticula were present, one close to where the obstruction occurred. A diagnosis of carcinoma of the colon was suspected. At operation the patient had an annular carcinoma.

Figure 3a shows the obstructed lesion before operation and Figure 3b shows the result after the operation, with the diverticula still present. This patient now has normal bowel movements, has gained weight, and is back to work.

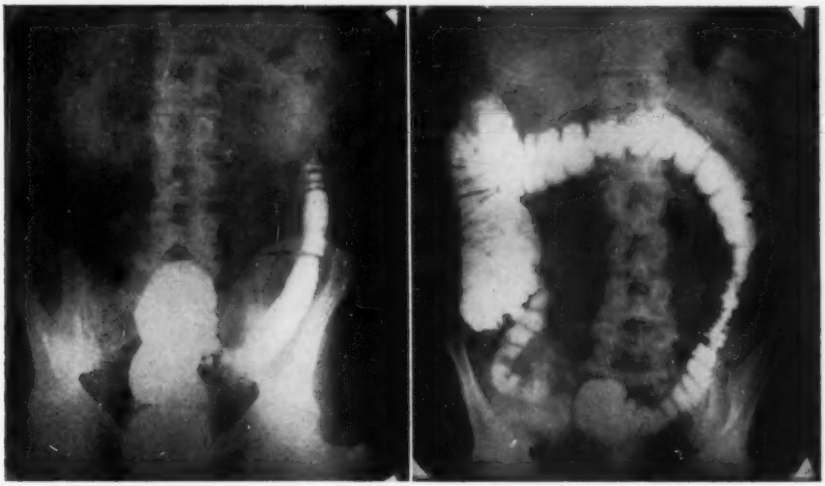

Fig. 3a Fig. 3b

There are three prominent symptoms of diverticulitis which also exist with carcinoma of the sigmoid or descending colon. There is pain in the left lower quadrant, change in the bowel habits and rectal bleeding, and in diverticulitis we also have cramp-like pains, rise in temperature and sometimes an increase in pains after a bowel movement. The symptoms of obstruction may develop in both cases, together with colic pain, distention, anorexia and vomiting.

Table II shows the symptoms that occur in both diverticulitis and carcinoma. Diverticulitis must also be differentiated from tuberculosis of the colon, acute appendicitis, ulcerative colitis or pelvic inflammatory disease. According to Colcok and Sass[4] practically all cases of colonic diverticulitis and approx-

imately 25 per cent of all cases of colonic cancer occur in the sigmoid colon; though an accurate differential diagnosis in these two disorders is required.

Diverticulitis is noted, however, by a higher percentage of patients with symptoms of abdominal pain (74 per cent) in comparison to the frequency of this complaint in patients with colonic carcinoma (26 per cent). Colic-like pain also occurs with a far greater incidence in diverticulitis patients (80 per cent) than in patients with carcinoma (38 per cent). On the other hand, rectal bleeding is significantly higher in carcinoma (64 per cent) than in diverticulitis (22 per cent). Constipation is more common in carcinoma, whereas nausea, chills, vomiting and fever occur more frequently in diverticulitis. Rectal or abdominal tenderness is found more frequently in diverticulitis.

Figure 4 shows a diverticulosis with diverticulitis, with the largest diverticula, I believe, I have ever seen in a patient. This patient was advised to have an operation for its removal and at surgery a fibroid uterus was attached to the sigmoid colon and diverticula. This was freed but not removed.

TABLE II

PROMINENT SYMPTOMS OF DIVERTICULITIS AND CARCINOMA

Pain in the left lower quadrant
Change in bowel habit
Rectal bleeding

The therapy of diverticulitis may be summarized as follows: 1. Bed rest during the acute attack and sometimes local application of heat to the abdomen as a means of relieving the pain.

2. A diet that is extremely low in its roughage content, with restriction of the diet to surgical liquids during the most acute phase of the disease.

3. Mineral oil preparations to regulate bowel functions. Often an enema each day with mineral oil will give relief even to the patient who has marked diarrhea.

4. Sulfa preparations have been a great help in allaying the inflammation, and even penicillin by injection may be of some assistance, together with some of the antibiotics, intravenously.

5. Mild sedation and antispasmodic drugs are of value. I avoid any use of morphine or its derivatives.

6. Infusions will be of help if there are frequent loose stools and there is a possibility of any electrolytic imbalance. If nausea and vomiting are present atropine by injection may be of help in allaying some of the spasms.

7. I have found that bismuth subnitrate or Kaopectate can be used at a later date to control the gas and diarrhea.

8. If complications develop, then your surgeon must be called to treat these.

A question arises–what *not* to do with diverticulosis or diverticulitis.

1. Do not feed your patients roughage, such as peanuts, raisins, lettuce, celery, cabbage, pork or veal, etc.

2. Do not give strong laxatives, soap enemas, or colonics.

3. Advise the X-ray Department not to use castor oil or licorice powder prior to barium enema.

4. Avoid narcotics.

5. Do not force air into the bowel through the sigmoidoscope or when the patient is being x-rayed.

Fig. 4

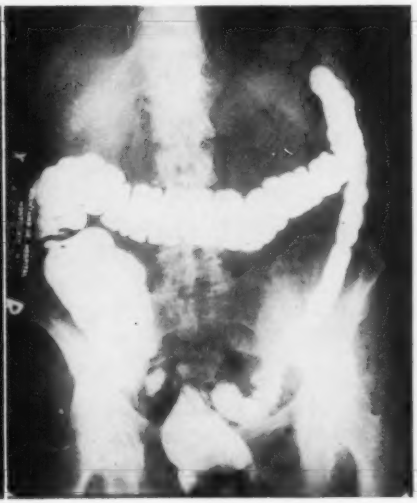

Fig. 5

Conclusion

Figure 5 shows the presence of diverticulosis in a patient who was treated for this condition and did not improve.

If only diverticulosis is present and there are other gastrointestinal symptoms, search for another cause. This patient was found to have a gastric ulcer and after treatment the gastrointestinal symptoms all subsided.

We must constantly be on the lookout for conditions other than diverticulitis if the patient has not recovered after proper treatment for either diverticulosis or diverticulitis.

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CARCINOMA OF THE SIGMOID COLON DISCOVERED DURING EXAMINATION FOR ACUTE INTUSSUSCEPTION OF THE SIGMOID

Case Report

HARRY A. FEIGENBAUM, B.S., M.D.

Jamaica, N. Y.

Mrs. H. Z. was referred for consultation because of acute colicky lower abdominal pain of three days' duration accompanied by passage of blood by rectum both bright red and dark and mixed with mucus but no stool.

The past history revealed the following interesting facts. For two years, since 1952, Mrs. Z. complained of weakness and stubborn constipation. There was never any blood noted in the stool nor was there any change in the bowel habit. She was hospitalized for study. Blood count revealed a moderate secondary anemia, urinalysis was negative, and rectal examination was also essentially negative except for some external hemorrhoidal tags. Sigmoidoscopy was done as were barium enema and gastrointestinal x-ray studies. These too failed to report any significant pathological finding. The patient was discharged from the hospital and treated with diet, hematinics and antispasmodics. The response was negligible. The patient's status remained unchanged up until six months ago when she noted for the first time that her stools had become loose and were mixed with mucus. Urgency to defecate too had become noticeable. Mrs. Z. was again hospitalized and again the sigmoidoscopic, barium enema and gastrointestinal x-ray studies were noncontributory. The patient was treated symptomatically. Her appetite began to decline as did her weight.

In December 1954, two years since her initial complaints, Mrs. Z. developed acute colicky lower abdominal pains and pain in the rectum accompanied by passage of blood mixed with mucus but with no stool. The desire to defecate was constant. Examination revealed a pale, thin, anxious, asthenic, slight female of 51 years of age. She was in moderate distress. She was placed in the lateral Sim's position. Anal inspection showed a few external hemorrhoidal tags. No blood was noted coming from the anus. Digital examination was very significant. A smooth sausage-like mass was felt protruding through the rectosigmoid valve. It was firm but resilient, nonpulsating and slightly tender and extending down almost to the anal orifice. On sweeping the index finger around, an ulcer with almost cartilaginous borders, about the size of a dime was felt in the presacral ampullary region of the rectum, on the posterior wall of the presenting mass. Blood was noted on the examining finger. An anoscope was introduced and the mass appeared to be intussuscepted sigmoid colon bearing an indurated ulcer on the posterior wall. Biopsy was taken from the ulcer crater and several areas

Department of Anorectal Surgery, the Jamaica Hospital, Jamaica, N. Y.

of the border. The crunching sound of the forceps is almost pathognomonic for malignancy. The patient was then placed in the knee-shoulder position and a sigmoidoscope introduced. The sigmoid was gently reduced by the sigmoidoscope and the assumed position and the patient obtained immediate relief of her abdominal pains. The ulcerated mass was then located at 17 cm. from the anal verge. The sigmoidoscope was then partially withdrawn and the patient asked to bear down. The sigmoid came down very easily again.

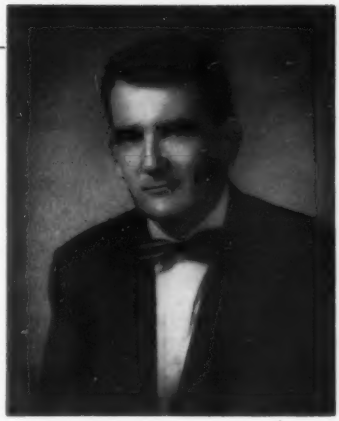
The pathological report was adenocarcinoma of the sigmoid colon, poorly differentiated and invasive.

The patient was operated and had an anterior resection of sigmoid and left colon performed. To date she is doing well.

Comment:—This case is interesting from several points of view. Our present diagnostic methods for detecting early cancer of the bowel leave something to be desired. In this instance the patient had been sigmoidoscoped twice and had two barium enema studies done. That a barium enema study will fail to detect a bowel lesion in some cases is established. It would appear that in the course of two years some abnormality would have been detected on sigmoidoscopy.

Intestinal polyps are frequently reported as initiating intussusception. In this case we cannot incriminate this small ulcerating carcinoma as producing the intussusception of the sigmoid colon. The long mesosigmoid was largely responsible.

Conclusion:—A case of carcinoma of the sigmoid colon discovered as an incidental finding during examination of a patient for acute intussusception of the sigmoid colon is reported. Shortcomings of the barium enema study for lesions of the colon are again noted. The digital and sigmoidoscopic examination properly performed are still the first means of attack for the early detection of carcinoma of the rectum and sigmoid colon. Their value cannot be overemphasized.



President's Message

The progress report of the American College of Gastroenterology shows that the inaugural years have been years of constant advancement. It has been particularly heartening to me to note the disappearance of sectionalism and provincialism; our membership comprises men from many states, and of many specialties and creeds.

Total membership in October 1953, was 780 men of whom 295 were Fellows and Life Fellows. As of March 1956, total membership was 811, of whom 332 were Fellows and Life Fellows. Membership declined from 344 to 315 but Fellowship is on the incline at an increasing ratio.

In October 1954, the College was represented by membership in 36 states, with 14 appointed governors. In March 1956, the College was represented in 39 states, with 23 governors. Percentagewise, our gains in membership were shown in the following states: Alabama, Washington, D. C., Illinois, Iowa, Louisiana and Texas. An exceptional membership campaign in Illinois resulted in an outstanding increase from 25 in 1953 to 51 in 1956. California, Connecticut, Michigan, New Jersey, New York, Tennessee and Wisconsin showed relatively little changes in total enrollment. A decrease in our membership was seen in Florida, Massachusetts, Missouri, Ohio, Pennsylvania and Rhode Island. The compiling of this and similar progress data on the American College of Gastroenterology is beneficial and should be recorded at intervals of every six months. The data included in this report should be supplemented with information on the number of pages in the journal, yearly profit of the journal, number of chapters, specialty data and college membership, with a breakdown on the convention course and regional meeting attendance. This is properly the realm of the Secretary-general and the mechanism for collection and recording could best be handled by Dr. Ferguson.

As far as expansion of our organization is concerned, I feel that local societies of gastroenterology, more frequent regional meetings and inauguration of memorial lectureships will be most productive. The time for improving local societies is now and the only rigid requirement that I can think of is that members of local societies must be members of the American College of Gastroenterology.

I. T. Nix

NEWS NOTES

Course in Postgraduate Gastroenterology

The American College of Gastroenterology announces that its Annual Course in Postgraduate Gastroenterology will be given at The Roosevelt in New York City, on 18, 19, 20 October 1956.

The Course will again be under the direction and co-chairmanship of Dr. Owen H. Wangensteen, Professor of Surgery of the University of Minnesota Medical School, who will serve as surgical co-ordinator and Dr. I Snapper, Director of Medical Education, Beth-El Hospital, Brooklyn, N. Y., who will serve as medical co-ordinator. Drs. Wangensteen and Snapper will be assisted by a distinguished faculty selected from the medical schools.

The subject matter to be covered in the Course, from a medical as well as surgical viewpoint, will cover, essentially, the advances in diagnosis and treatment of gastrointestinal diseases and a comprehensive discussion of diseases of the mouth, esophagus, stomach, pancreas, spleen, liver and gallbladder, colon and rectum, with special studies of radiology and gastroscopy.

For further information and enrollment write to the American College of Gastroenterology, 33 West 60th Street, New York 23, N. Y.

Correction

The dosage of Antrenyl shown in Table II on page 254 of the article "Experimental Methods for the Evaluation of Therapeutic Agents in Peptic Ulcer" by Dr. Frank P. Brooks which appeared in the September 1955 issue, is incorrect.

The correct dosage for Antrenyl should be: 500 *micrograms/kg.*

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GASTROINTESTINAL TRACT

EFFECTS OF DORSOLUMBAR SYMPATHECTOMY ON PEPTIC ULCERATION: Ian Macpherson and A. A. Fitzgerald. Brit. M. J. 4923:1185 (14 May), 1955.

Extensive dorsolumbar ganglionectomy and splanchnicectomy carried out for a number of symptom-complexes necessarily interrupts the sympathetic nerve fibers supplying the stomach. This might result in harmful effects by masking symptoms of peptic ulceration so that frequently lesions in the gastrointestinal canal are found only when complications, such as pyloric obstruction, perforation, or hemorrhage calls attention to the conditions.

A case is cited in which bilateral dorsolumbar ganglionectomy with splanchnicectomy was performed for hypertension. After this surgical procedure a progressively active duodenal ulcer developed with pyloric stenosis with subsequent complication of a jejunal ulcer which perforated. Pain was only experienced when the rupture occurred. This served to illustrate how intradigestive tract pathology may develop without pain and thus remain unrecognized after the severance of sympathetic nerve fibers. This stresses the need to thoroughly investigate any vague abdominal symptoms and signs in order to diagnose digestive tract lesions in the absence of usual nervous innervations.

REGINALD B. WEILER

EFFECTS OF VAGOTOMY ON AUTONOMIC BALANCE: Kenneth B. Little. Psychosom. Med. 17:227 (May-June), 1955.

This study conducted with 40 male peptic ulcer patients indicates that vagotomy effects marked changes in bodily function resulting from a reduction of sympathetic activity. But there are other reasons for the marked physiological response to vagotomy which are less apparent. Gastric resection alone is capable of altering relative sympathetic responses. The chief reason for such widespread differences might represent a readjustment following stress. Pain, especially of a chronic nature, constitutes a psychological stress which renders the organism especially reactive to added stresses. There would be erected, as a defensive measure against traumata in those exposed

to chronic insult, an especially active susceptibility to all stress so that any stimulus associated with potential additional threats of this nature would at once provoke an overreactivity as a protective device. Consequently in the ulcer patient whose very pathology psychologically is interpreted as a threat of destruction, would be in such a state of defensive preparedness that all stimuli of a stressful type would be warded off by an overreaction of bodily defenses.

REGINALD B. WEILER

HISTOPATHOLOGIC STUDIES OF GASTRIC ULCER-CARCINOMA: I. ON THE ORIGIN OF GASTRIC ULCER-CARCINOMA: Susumu Majima. Tohoku J. Exper. Med. 62:53 (25 June), 1955.

From a group of 86 cases of ulcer-carcinoma of the stomach, Majima reports histopathologic studies of 18 cases in which the ulcer base was free of carcinoma. Half of the lesions were found in the *corpus ventriculi* and the remaining nine at the *pars pylorica*. Using the serial section method, the author concluded that ulcer-carcinoma seems to originate from regenerative epithelium of atypical proliferation. In 11 of the 18 cases with early ulcer-carcinoma, multicentric development of cancer foci were demonstrated at the ulcer margin or in the mucus membrane apart from the ulcer margin. In five of the six remaining cases, cancer foci extended to surround the ulcer margin completely or almost completely being thus suggestive of the fusion of multicentrically developed cancer foci.

JOHN M. MCMAHON

HISTOPATHOLOGIC STUDIES OF GASTRIC ULCER-CARCINOMA: II ON THE GROWTH OF ULCER-CARCINOMA: Susumu Majima. Tohuku J. Exper. Med. 62:63 (25 June), 1955.

In a histopathologic study of 752 cases of gastric cancer and 293 cases of gastric ulcer, 86 of ulcer-carcinoma (54 from the former, 32 from the latter) were found by Majima. Thus the incidence of ulcer-carcinoma was 24.9 per cent in gastric ulcer and 10.9 per cent in gastric cancer. From a general survey of various stages of ulcer-carcinoma from early to advanced, the author made the following conclusions with reference to the process of its growth: Cancer foci which had developed multicentrically at the ulcer margin, extend independentally through the submucus layer and the free ends of the muscular layer to the subserous layer and invade the callous tissue making up the ulcer base. Sideward infiltration of the superficial part of the base and the free omentum tissue also takes place. Therefore, in the stage showing carcinomatous proliferation at the ulcer base, cancer tissue often causes infiltration beyond the serous membrane of the stomach. For this reason in ulcer-carcinoma, an unfavorable prognosis is to be given for its size. Each type of histological picture as classified by Petersen and Konjetzny were found in 86 cases.

JOHN M. MCMAHON

ON THE POSTOPERATIVE PROGNOSIS IN ULCER-CARCINOMA OF THE STOMACH: S. Majima, J. Katami, N. Kurakake and N. Hoshi. Tohoku J. Exper. Med. 62:75 (25 June), 1955.

Majima and his associates report on an investigation of late results of gastrectomy in 60 cases and a comparison is made between these results and the histopathologic findings with the resected specimens. The latter have been classed in four groups according to the depth of carcinomatous infiltration. In those cases, graded one to three, in which infiltration of carcinoma originated at the ulcer margin, it was confined to a small part of the base or to the subserous layer. Late results of gastrectomy have been favorable, whereas the results have been unfavorable in the group of cases, grade 4, in which the infiltration extended to a great part of the ulcer base and beyond the serous membrane. The authors also feel that the postoperative prognosis for ulcer-carcinoma may be said to be as unfavorable as for gastric cancer, when the survival rates, in successive years after operation are compared.

JOHN M. MCMAHON

OCCURRENCE OF GASTRIC CANCER AMONG PATIENTS WITH PERNICIOUS ANEMIA AT THE BOSTON CITY HOSPITAL: Norman Zamcheck, Ernest Grable, Allyn Ley and Leona Norman. New England J. Med. 26:1103 (June) 1955.

This is mainly a statistical study of the incidence of gastric cancer in patients with pernicious anemia with a comparison with other such studies. The authors were able to demonstrate a definite relationship between gastric cancer and pernicious anemia. Cancer may occur anywhere from 0 to 12 years after the diagnosis of pernicious anemia is made. There is evidence to suggest that gastric cancer may precede a pernicious anemia-like picture. Because cancer may develop years after the diagnosis of pernicious anemia is made (In this group, the average age was 7 years), the authors suggest that screening tests should be used to follow cases of pernicious anemia since the usual means of study would be too expensive to be practical. They suggest stool examinations for occult blood at monthly intervals and examination of gastric cytology at 3-6 month intervals. If either of these procedures produce suspicious cases, then further study by x-ray and gastroscopy should be done. Ten per cent of their cases of pernicious anemia had gastric cancer by the time they died or left the clinic, presumably dead.

ABE ALPER

SURGICAL MANAGEMENT OF MASSIVE ACUTE UPPER GASTROINTESTINAL HEMORRHAGE: Claude E. Welch, Arthur W. Allen and Gordon A. Donaldson. New England J. Med. 252:921 (2 June), 1955.

Patients with gastrointestinal bleeding are admitted to the surgical wards of the Massachusetts General Hospital. Mild, moderate and massive bleeding is distinguished by the amount of blood loss and the need for replacements. Theoretically massive bleeding denotes the loss of more than 40 per cent of the total circulating blood mass. However, as blood volume studies are usually not available a fall of hemoglobin to 70 grams per 100 c.c. or the need for more than five units of blood constitute massive bleeding and are mostly indications for emergency surgery. Ulcer is by far the most important cause of massive hemorrhage. Bleeding from hiatus hernia and gastritis is usually self limited. The peptic ulcer may be in the stomach, the duodenum, or the esophagus. Early x-ray examination with Hampton's nonpalpation technic is frequently required while esophagoscopy and gastroscopy are only rarely used. Elderly patients, patients with recurrent hemorrhages, those with gastric ulceration, or with associated cardiac, cerebral and renal ailments have a better chance of survival if they are operated early. If no exact preoperative diagnosis has been made and the stomach appears full of blood at the operation it is opened and carefully examined. Rarely no cause of bleeding can be found and the entire small bowel must be investigated with great care. If it too is normal subtotal gastric resection is done. Surgical mortality of the last five years in massive bleeding cases is greater than it used to be in previous similar periods. This appears alarming on first thought but it is due to the surgical attack of more lesions previously considered inoperable; furthermore, it is caused by the higher age of the hospital population and the fact that massive gastrointestinal hemorrhage occurs most frequently in the elderly. Finally, it is due to the difficulty to prevent postoperative fatal complications such as, aspiration, pneumonia, pulmonary embolism, persistence of shock or internal hemorrhage, pancreatitis, leakage of the duodenal stump, subphrenic abscess and peritonitis, stomal obstruction with malnutrition, severe electrolyte disturbance and coronary or cerebral thrombosis.

H. B. EISENSTADT

EARLY ROENTGEN EVALUATION OF GASTROINTESTINAL BLEEDING: Albert M. Kohn, Gene W. Sengpiel and Joseph F. Wepfer. Wisconsin M. J. 54:331 (July), 1955.

This is a study of 123 patients who had roentgen examinations to determine the cause of bleeding. According to the authors, the sole reason for not doing the examination was the presence of severe shock and these patients were examined only once.

There are two tables given, one having to do with the type of lesion found and

it is pointed out that no lesion was found in 27 per cent of the 123 cases which compares well with the results at Cleveland in a comparable study but rather poorly with results in Boston. We do not know, nor is it stated whether the Boston series had only one single examination or multiple.

In the Boston series gastritis was considered a roentgen diagnosis whereas in this series, gastritis was not considered. This may explain the discrepancy.

Common diseases commonly occur and the lesions found responsible for upper gastrointestinal hemorrhage are: 1. Duodenal ulcer; 2. gastric ulcer; 3. esophageal varices.

A description of the procedures is given. The authors conclude that early examination entails no appreciable risk to the patient and recommend it.

IRVIN DEUTSCH

PEPTIC ULCER IN GENERAL PRACTICE: David I. Finer and John Fry. Brit. M. J. 4932:169 (16 July), 1955.

The incidence, morbidity and response to treatment of peptic ulcer of nonhospitalized patients in a combined practice of 10,000, shows a 5-year total of 177 cases, with 53 giving a history of less than 5 years, in an age range of 20 to 70.

Three lines of treatment were used, 1. surgical and medical for 5-year history cases, with 31 surgical and 93 medical resulting in 37 per cent requiring no further treatment, 77 per cent requiring less attention than prior to therapy. 2. Surgical treatment only (a) 27 gastrectomies, (b) 4 gastrojejunostomies, 24 requiring no further attention, 3 needing some adjuvant treatment. 3. Medical care only, due to other complicating diseases, of these 12 patients, 70 per cent requiring less attention with 30 per cent requiring no additional therapy.

During the five-year study there was an incidence of 18 per cent in bleeding, and 10 per cent in perforation.

J. EDWARD BROWN

GASTROINTESTINAL ULCERATION AND NONULCERATIVE DYSPEPSIA IN AN URBAN GENERAL PRACTICE: S. Lipetz, S. A. Sklaroff and Lilli Stein. Brit. M. J. 4932:172 (16 July), 1955.

Twenty year study in incidence of peptic ulcer in a practice of 5,331, equally divided, male and female, made up of a working class with a high proportion of elderly, showed greatest percentage of lesions in the 40 to 44 age bracket, 61 cases, next highest, 35 to 39, 45 cases, with 45 to 49 showing 32 cases.

Over the study years the total number of cases was 323 with 17 per cent giving familial history of ulcer, 52 out of 56 being duodenal, and occurring in but 15 families.

Total incidence of peptic ulcer was 4.7 per cent, among males, 7.0 per cent and in females 2.4 per cent, perforation was placed at 19.2 per cent, with two deaths, hematemesis accounted for 16.4 per cent.

After treatment, relapse occurred in 43 per cent of the duodenal cases, and in 26 per cent of the gastric ulcer cases.

Evaluation of ulcer against chronic dyspepsia showed ulcer 3 times more prevalent than dyspepsia.

J. EDWARD BROWN

FOREIGN BODIES IN THE GASTROINTESTINAL TRACT: Robert T. Gants and Jack B. Jay. U. S. Armed Forces M. J. 6:987 (July), 1955.

Of the 75 per cent of swallowed foreign bodies which pass through the esophagus, the great majority lodge either in the stomach or duodenum. Complete passage can be expected if the object passes the duodenum, although a few cases have been reported lodged in the appendix, at the ileocecal valve, or in a Meckel's diverticulum.

Ordinarily there is a long latent period of approximately two or three weeks between the time of ingestion and the onset of clinical signs of a complication. Perforation is unusual and the process takes place slowly, being walled-off by inflammatory changes. Symptoms consist of low-grade fever, mild abdominal pain, and localized tenderness. Minor bleeding and vomiting may also occur. Because of the lack of symptoms and their relative insignificance, history is very important in diagnosis. For-

tunately almost all foreign bodies are radiopaque and roentgenologic examinations are also useful in following the progress of the foreign body through the gastrointestinal tract.

Management includes careful examination of the stools daily in the search for the foreign body. The patient should remain on a normal diet and no laxatives should be administered. Strenuous physical activity should not be permitted.

Indications for surgery include roentgenologic evidence of retention of the foreign body in one position for several days; foreign bodies of such size and shape that passage is impossible and clinical evidence of perforation or obstruction.

The authors present three case reports by way of illustration.

JOSEPH E. WALTHER

REVIEW OF FIFTEEN YEARS' EXPERIENCE WITH GASTRECTOMY IN A COMMUNITY HOSPITAL: I. ULCER: Paul R. Hinchey. New England J. Med. 253:176 (4 Aug.), 1955.

Gastrectomy for duodenal ulcer is being done much more frequently today than used to be the case.

Gastrectomy is proposed to patients with massive bleeding who have previously bled or have a long ulcer history or pyloric obstruction. Gastrectomy is also advocated for patients with bleeding gastric ulcer and persistent gastric ulcer. The possibility of carcinoma must be considered in all cases of persistent gastric ulcer. One must not rely on the size, duration or location of the ulcer to rule out malignancy. Gastric analysis for acidity and cell study should be routine in all cases of gastric ulcer. Gastrectomy can be very helpful.

BERNARD STERN

ESOPHAGUS

CONGENITAL ANOMALIES OF THE ESOPHAGUS: Francis S. Gerbasi. U. S. Armed Forces M. J. 6:843 (June), 1955.

The author classifies congenital anomalies of the esophagus into the following types and then discusses each one.

1. Atresia of the esophagus without fistula. X-ray will show gas in the bowels, but diagnosis is confirmed by passing a catheter into the esophagus until it meets an obstruction.

2. Atresia with tracheoesophageal fistula. This is the most common anomaly. A catheter cannot be passed into stomach. Presence of air in the gastrointestinal tract indicates connection between bronchus and lower esophagus.

3. Congenital tracheoesophageal fistula without atresia occurs infrequently and majority take place above the bifurcation. Treatment is surgical division of fistula and closure of divided ends.

4. Congenital stenosis. The majority show evidence of obstruction before they are 15 days old. Vomiting of undigested food is effortless and not projectile. Esophagram confirms diagnosis. Esophagoscopy will show exact nature of stenotic area and degree of esophagitis. Dilatation should be attempted first and if not successful excision with end-to-end anastomosis.

5. Congenitally short esophagus. This condition is very rare and seldom troublesome. Treatment consists of bland diet, dilatation and lastly phrenemphraxis.

6. Duplication of esophagus may be intramural or extramural, the latter being much more common. Treatment is transpleural excision.

7. Chalasia is a persistent relaxation of the cardioesophageal junction. X-ray confirms diagnosis. Barium is seen to go from the stomach into the esophagus on inspiration and when pressure is applied to abdomen. Treatment consists of keeping child in upright position for 30 minutes after eating. Condition corrects itself after 3-4 weeks.

8. Achalasia may be congenital or acquired. X-ray establishes diagnosis. Treatment—antispasmodics give poor results. Surgery—as a last resort is extramucosal esophagocardiomyotomy.

LOUIS K. MORGANSTEIN

PERFORATION OF THE ESOPHAGUS: John E. Summers, Arthur L. Stanley and Christopher J. Stringer. J. Michigan M. Soc. 54:677 (June), 1955.

Perforations of the esophagus are either traumatic or spontaneous. Most traumatic perforations follow instrumentation or swallowing of foreign bodies, especially pieces of glass, fish, chicken bones and safety pins. Rare causes are severe external injury, rupture of aortic aneurysm, extrapleural pneumothorax and various intrathoracic operations.

Spontaneous perforation of the esophagus is supposed to be due to a combination of excessive intraesophageal pressure from vomiting together with acid pepsin digestion. It occurs most frequently in middle-aged alcoholics. Perforation of the cervical esophagus follows mostly instrumentations and is characterized by pain, dysphagia, local tenderness, subcutaneous emphysema and rigidity of the cervical spine. X-ray of the neck reveals subcutaneous air and forwards displacement of the trachea. Treatment is "cervical mediastinotomy" with drainage of the visceral space.

Perforation of the mid-esophageal region is usually due to foreign bodies. Pain in the chest, dysphagia, chills and fever occur. When the lesion is confined to the mediastinum only widening of this structure is seen on the x-ray picture. More often rupture into the pleural cavity occurs with shock, cyanosis, dyspnea, subcutaneous emphysema, pneumothorax, pleural effusion. Transpleural drainage is then the surgical treatment of choice. Perforation of the lower end of the esophagus is usually due to dilating instruments or is spontaneous. It is frequently mistaken for ruptured abdominal viscus but shows subcutaneous emphysema, pneumothorax and gastric contents in the pleural cavity. Immediate transpleural surgical treatment is required. One case of mid-esophageal perforation is described where x-rays showed a slightly opaque piece of glass swallowed by a child and a unilateral pneumothorax but where radio-opaque material taken by mouth did not reveal any extravasation.

H. B. EISENSTADT

THE SURGICAL TREATMENT OF BLEEDING ESOPHAGEAL VARICES: Robert R. Linton. West J. Surg. 336 (June), 1955.

Esophageal varices represent one of nature's attempts to create a shunt between the portal and systemic venous circulations. In addition to the increased pressure of the portal system hypervolemia is responsible for their development. The cause of their rupture is unknown. Peptic esophagitis has been suggested by Wangensteen but is usually not found at the time of surgical transesophageal exposure. Only puncture-like openings suspicious of mechanical trauma are seen. Mortality of varices of extrahepatic portal hypertension is much smaller than of those associated with cirrhosis, mainly because about 50 per cent of the latter cases die before definitive surgical therapy can be attempted. Gastro-esophageal balloon tamponage is the method of choice for initial emergency treatment. However, this method becomes dangerous if maintained for a longer period of time. Therefore, transpleural trans-esophageal ligation of the varices should follow if the bleeding persists. This will stop hemorrhage for several weeks and allow proper preparation of the patient for a shunt operation. In a group of 24 patients there was only one death attributable to such a ligation. Every patient with bleeding varices should be considered a candidate for surgical shunt as a definite form of therapy. This can be done in all cases of extrahepatic block but only in half of those with intrahepatic obstruction because a relatively good liver function is required. This excludes patients with serum albumin below three gram per cent, uncontrollable ascites and markedly abnormal liver function tests. All patients with extra- and 60 per cent of those with intrahepatic obstruction that could be subjected to surgery obtained a splenorenal shunt while only a minority had a direct portocaval communication. Ninety per cent of those cases were alive at this survey one to seven years after operation.

H. B. EISENSTADT

STOMACH

PRESENT-DAY PROBLEMS OF SURGERY OF THE STOMACH: Werner Wachsmuth. Arztliche Wchnschr. 10:313 (8 Apr.), 1955.

In the opinion of the author it is impossible to give a definite answer regarding the absolute value of any given surgical method employed today in treating peptic and duodenal ulcer. It may take many years before such an operation par excellence has been found. As conservative surgery did not fulfill the expectations the author still considers subtotal gastrectomy as the standard procedure. In his opinion peptic ulcer is primarily a medical disease and only selected cases are subjected to operation. The indications are: 1. perforated ulcer, 2. presence of organic stenosis, 3. *ulcus callosum*, 4. suspicion of malignant degeneration, 5. massive gastric hemorrhage and repeat hemorrhages, 6. chronic peptic ulcer—especially in people above 40—if and when at least two medical attempts to cure the ulcer have not proven successful.

Perforated ulcer is, in the opinion of the author, a purely surgical disease. If a primary resection is possible, that is if the perforation is of less than six hour's duration and the general condition of patient is good, this procedure should be done. Otherwise—especially in juvenile patients—simple closure is the method of choice. Regarding the operation of severe gastric hemorrhage the author has today the generally accepted point of view that before surgical interference all efforts should be made to improve the patient's condition by conservative methods. On the other side the author is in favor of blind resection, when a bleeder cannot be located.

Previous experience and newer scientific research established the fact that disturbances of protein-iron metabolism are caused by the exclusion of the duodenum in the Billroth II methods of operation. Therefore, if possible, the author prefers the B-I technic. He also advises to do a fundectomy with esophagoantral anastomosis in higher-up located ulcera. Different technics, their pros and cons, are described in detail. It is of interest to note that the author does vagotomy only in case of jejunal, postgastrectomy ulcer, using the abdominal approach.

In the second part of his paper the author discusses the surgeon's problems in handling gastric carcinoma. The different technics of partial resection, total gastrectomy, and gastric replacements are explained. Unfortunately the author's pessimistic outlook is shared by a great number of physicians. His, and for that matter everybody else's point of view, can best be summarized as follows: Only in the very early stages of gastric carcinoma can one expect a cure. As to methods: be as radical as necessary, as conservative as possible, and do not attempt to accomplish the impossible.

HANS JOSEPH

"PHANTOM PAINS" AFTER STOMACH RESECTION: Bela Gimes. Fortschr. Roentgen. 82: (May), 1955.

Four hundred patients with different complaints who underwent a gastric resection because of ulcer were examined. In 62 cases the patients have exactly localized pains on the right side of the resected stomach stump corresponding to the spot where the ulceration had been localized in the resected part. Radiologically demonstrable changes which might explain these pains were not found. To explain this sort of pain we must suppose a mechanism similar to that of the phantom pains of amputated extremities. The phantom pain of the patients with gastric resection must be regarded as a pain, which appears after the *plexus pyloricus* has been severed and arises by projection into the preoperative area.

FRANZ J. LUST

THE BELCHER GASTRECTOMY FOR PEPTIC ULCER: D. G. MacQueen. Canad. M. A. J. 72:666 (1 May), 1955.

The author's series of cases ranged over a period of eight years and he states that 98 per cent of the patients were well pleased with the end-results of their operation, although 70 per cent of all cases are not up to par physically in spite of

adequate intake of food. Many of these cases (25 per cent) were frank "dumpers". Obviously there is gross interference in digestion and absorption of food.

The Belcher operation removes 75 per cent of the whole stomach including all the antrum and pylorus, and anastomoses with the duodenum. Normal suspension and support of the gastric remnant is provided and it is thought that gastric emptying time is slowed down. It was not found necessary to mobilize the duodenum. Sixty-seven cases are reported with no deaths or serious complications. It is not the aim of this operation to secure a state of achlorhydria, although this condition prevails in some of these cases.

JOHN E. COX

IMMEDIATE PARTIAL GASTRECTOMY FOR PERFORATED PEPTIC ULCER: B. C. Rowlands and P. A. King. Brit. M. J. 4924:1254 (21 May), 1955.

In the period, January 1952-June 1954, 54 cases of perforated peptic ulcers were treated by the authors and since then an additional 15 cases were also cared for. Prior to this time, the authors impressed with the inconvenience to the patient of disabling symptoms following simple closure of the perforated peptic ulcer and the increased technical difficulties at the time of the second operation, decided to treat certain selected cases by immediate partial gastrectomy. Although the treatment of a perforated peptic ulcer is a life-saving measure and many feel that the simplest procedure (closure) is all that should be attempted, there are many supporters who contend that immediate partial gastrectomy is a safe procedure. Many surgical clinics have statistics indicating that the mortality rate from immediate partial gastrectomy is no greater than that of simple closure. If hemorrhage co-exists with perforation, the combination is dangerous and is most satisfactorily dealt with by immediate partial gastrectomy. The authors' criteria for determining fitness for immediate partial gastrectomy was to assess the patient's general condition as the main element as well as the history of concomitant ematemesis, ulcer dyspepia, history of previous perforation, etc., and no arbitrary time interval from the onset of symptoms was laid down, thus they encountered varying degrees of peritoneal soiling.

IRVIN DEUTSCH

PEPTIC ULCER: Edward A. Marshall and Morton Sass. Med. Times 83:552 (June), 1955.

This presentation describes a therapy utilizing unrestricted diet. This is accomplished by the immediate exhibition and adequate continuation of potent antacid-sedation mixtures.

The only other therapy employed is the use of milk at night. Adequate dosage is essential and remains unaltered for 4½ months. During this entire period night medication is maintained without remission.

In actively bleeding patients the "heavy plan" is started on admission and maintained for 24 hours. If bleeding is controlled, within 24 hours, the "half-heavy" schedule is substituted for 24 hours, and then switched to "quarter-heavy". Soft or liquid diet is started the first day but unrestricted diet is given from the second day on. Of 140 such cases only 8 bled more than 24 hours, for a 94.3 per cent success. The total mortality was 2 or 1.42 per cent.

In nonstenotic obstruction, first the stomach is emptied then the patient is placed on the heavy therapy for 24 hours while fasting; but following this the usual ambulatory regime is instituted including the full diet. In this series only 7 out of 201 cases treated failed to respond to the heavy plan. The only surgery performed was for 14 cases of organic stenosis, out of a total patient series of 1,500. Of these 89.3 per cent were duodenal ulceration, 9.2 per cent gastric, and 1.5 per cent marginal. Ninety-six cases were classified as failures.

REGINALD B. WEILER

INTESTINES

EOSINOPHILIC GRANULOMA OF THE DIGESTIVE TUBE: R. Picard, M. Hardy and J. Kerneis. Arch. mal. app. dig. 43:920 (Sept.), 1954.

Under the name of eosinophilic granuloma of the digestive tube two quite different disorders are described. The first, properly called eosinophilic granulomatosis is characterized by extensive eosinophilic infiltration of the stomach or of the small intestine. The second is, on the other hand, a tumoral formation, clearly delimited, this is Bolck and Vanek's *eosinophilic granuloblastoma*. It is this last disorder only which is studied here.

With the aid of various observations (Vanek, Bolck, Feyrter, Nunès) and the authors, the distinguishing features of tumoral eosinophilic granuloblastomas may be summarized as follows: 1. Three-fourths of the gastric cases are situated at the level of the antrum. 2. Sex is immaterial. 3. The age is the same as for cancer. 4. In the stomach the *clinical and radiological symptoms* are those of cancer. From the endoscopic point of view there is the picture of hypertrophic gastritis. 5. When they are intestinal they are always in the ileum and the picture is that of an invagination.

The pathological anatomy is simple: it is a granuloma formed from young or more mature histiocytes, bathing in a fundamental substance, few or abundant in quantity with fine or voluminous collagenous fibers. The main distinguishing feature is the sprinkling of the lesion by myriads of eosinophilia and the absence of malignancy (except in Holle's case with a sarcomatous development).

The pathogenesis is highly controversial. The authors believe it is a matter of an isolated tumor, and not allergic in character.

GUY ALBOT

RADIOSURGERY IN CASES OF CANCER OF THE RECTUM: Madame Parturier-Albot, M. Champeau and C. Frileux. Arch. mal. app. dig. 44:5 (Jan.), 1955.

It struck the authors that purely surgical treatment of cancer of the rectum, in spite of its outstanding success, could be improved upon.

The following is an outline of the treatment: 1. Contact radiotherapy alone for incipient or mucus type cancers which after an interval of up to 10 years have revealed 100 per cent cure. 2. Contact radiotherapy alone for indurated base type cancers with 95 per cent cures after intervals of up to 9 years. 3. It is above all in cancers of the granulating movable base type that the question of associated radiosurgical treatment is raised. 4. For cancers of advanced type *preoperative contact radiotherapy* could be contemplated in some cases.

The authors have thus treated in this manner 14 cases of cancer of the type with a movable granulating base: 1 was cured by contact radiotherapy alone. 2 were cured by contact radiotherapy followed by a limited simple exeresis (which gave histological proof of cure). 3 were cured by contact radiotherapy followed by widespread but conservative exeresis (and in which examination of the portion removed showed cure of the lesion). 1 case remained histologically doubtful after contact radiotherapy: (after limited exeresis it was deemed advisable to perform a large scale amputation). 7 cases finally proved fairly conclusively to be failures as far as contact radiotherapy was concerned and were later operated on in the usual way. It should be noted that in all these cases the operation took place in better conditions and that *a ganglion was never found to be affected in the portion removed.*

Out of 14 cases, 13 were cured with a time lapse of up to 6 years (in 4 cases). The 14th case was that of a patient who had undergone contact radiotherapy alone and relapsed after 3 years: she died from an operation on a pelvic bone cavity. This patient *did not present herself for examination for 3 years as she considered herself cured.* It is here a question of a psychological failure of the method: it may prove difficult to perform a second operation on patients who have improved considerably.

In conclusion, the authors think that, in incipient cancers of the rectum, contact radiotherapy and associated radiosurgical treatment should play an important role. It is however a method which is difficult and delicate to handle and it should occasion no surprise that a long period of trial and error has been necessary to perfect it.

GUY ALBOT

POLYPS OF THE COLON AND CANCERS: M. Vigoni. Acta gastro-enterol. belg. 18:152 (Feb.), 1955.

Vigoni presents arguments showing the malignant degeneration of benign polyps of the colon and the identical location of polyps and cancers in the same segments of the terminal colon. There is parallelism in both sexes. Frequent transformation of polyps into cancers are found. There is frequent association of polyps and cancer. The frequency of malignant degeneration in familial polyposis. Very often, multiple cancers of the colon are found. With these arguments, underlined with statistical data, one may think that almost every cancer of the colon is a degenerated polyp.

FRANZ J. LUST

IDIOPATHIC COLITIS ULCEROSA WITH PERNICIOUS ANEMIA OF THE BIERMER-ADDISON TYPE AND PSEUDO-ULCUS DUODENALE AND MULTIPLE NUTRITIONAL DEFICIENCIES: E. Oliver-Pascual, J. Sanz-Ibanez, F. Andolz, C. Elosegui, A. Oliver, J. Eleicegui and E. Castillo. Enferm. del appar. digest. 14:163 (March), 1955.

The writers report a case of multiple nutritional deficiencies of subclinical type whose symptoms were brought out by a probable viral infection which gave rise to idiopathic ulcerative colitis with ulceriform duodenitis. The latter condition was accompanied by periduodenitis and viral mesenteric lymphadenitis. The nutritional deficiencies together with the viral infection gave rise, by acting on a constitutional predisposition to pernicious anemia, with a severe megaloblastic mielosis due to deficiency of Vitamin B_{12} and hepatitis. Treatment with a diet rich in proteins and parenteral administration of Vitamin B_{12} were enough to attain clinical cure of the anemia and of the diarrhea. The lesions of the ulcerative colitis became latent.

FRANZ J. LUST

OPERATIVE RESULTS IN 59 CASES OF CROHN'S DISEASE. Julio Monereo Gonzales. Enferm. del appar. digest. 14:145 (March), 1955.

Gonzales proves the correlation between histology and macroscopic anatomy in Crohn's disease, and the importance of both examinations, in order to establish a prognosis. The author reports 59 cases operated on by him at the Philadelphia Graduate Hospital. These were followed-up for over five years. He concludes that exclusion operations are far superior to resection. In his opinion, Crohn's disease is malignant in character in a large number of cases. This idea is based on the follow-up of patients for a long time. Most papers published in medical literature are not concerned with patients followed-up for several years after they were operated upon, which is misleading in estimating the prognosis.

FRANZ J. LUST

OXYURIS VERMICULARIS: Heien B. Pryor. J. Pediat. 46:262 (March), 1955.

It has been estimated that over 200 million persons in the world harbor oxyuris. There is a higher incidence of infestation among people who live in institutions. It is usually a familial disease. Dogs and cats do not harbor pinworms in their gastrointestinal tract but carry them on their fur. Pinworm ova have been demonstrated on bedding, sleeping garments, hands, toys, furniture and floors and in house dust. They remain viable for days and weeks in cool, moist places. Since the female pinworm requires free oxygen for egg-laying examination of stools may not find ova. The female has to migrate to the anus and may deposit there as many as 11,000 ova of microscopic size. For this reason anal swab or Scotch tape methods must be used for finding eggs. Sunlight, ultraviolet lamp, good ventilation and drying of rooms will kill most eggs. Washable articles should be laundered in very hot water; dry oven heat sterilizes nonwashable toys. Rugs, furniture, drapery should be sunned on a dry, hot day. The room should be carefully vacuum-cleaned. Separate wash cloths for face and body safeguard against autoinfection.

H. B. EISENSTADT

MASSIVE RESECTION OF SMALL AND LARGE INTESTINE: J. E. Arata, R. B. Wilson and C. G. McEachern. A.M.A. Arch. Int. Med. 95:622 (April), 1955.

A 57-year old male had a resection of almost the entire small bowel and the right half of the colon with jejunotransverse colostomy following mesenteric thrombosis. After the operation a troublesome diarrhea occurred resistant to any treatment but gradually improved spontaneously. A few weeks after surgery the patient was in a satisfactory condition without using any drugs or any special diet. Only the intake of large amounts of fat had to be avoided because this promoted excessive calcium loss. It is the experience of the author—probably shared by many—that the tolerance of bowel resection varies considerably with each patient due to a great individual difference of adaptability to such a loss of gut. Some persons show severe deficiencies of absorption while others have very little abnormalities of bowel function.

H. B. Eisenstadt

OBSERVATIONS ON CANCER OF THE COLON AND RECTUM IN CONNECTICUT: Edward J. Ottenheimer and Ashley W. Oughterson: New England J. Med. 252:561 (7 Apr.), 1955.

This is a review of colonic malignancy by the Connecticut Tumor Registry representing 93 per cent of all general hospital beds of the state and reflecting the work of several hundred surgeons of both small and large communities. The conclusions drawn are that cancer of the colon and rectum is the most common cancer encountered. That it is on the increase, as is cancer in general, is well recognized. Forty-six and eight-tenths per cent (46.8 per cent) of cases are classified as localized, 30.8 per cent of cases are classified as regional (lymph nodes involved); 17.3 per cent showed remote metastasis. The percentage of patients in the various stages of the disease was approximately the same for all sites from ascending colon to rectum. Highly differentiated tumors tend to remain localized in all sites. Treatment should be radical in all cases of malignant polyps since this group probably represents cancer of the bowel in its earliest stage. In conclusion, the authors feel that as a result of this study, it might be said that whatever progress was made in the management of cancer of the colon in the past ten years was not the result of earlier diagnosis but rather a result of better and more radical surgical treatment. Further progress now will depend on the development of new technics for discovering cancer in its localized state where radical surgical treatment gives best results.

A. J. Brenner

LIVER AND BILIARY TRACT

LA CIRRHOSE METAICTERIQUE: Roger Crismer and Jacques Lambermont. Acta gastroenterol. belg. 18:114 (Feb.), 1955.

The authors draw attention to the frequence of "metaicteric" cirrhosis i.e. after viral hepatitis. Based on 10 cases in four years, they show the polymorphism of clinical symptoms, mostly a severe looking icteroascitic syndrome in the beginning. Hepato- and splenomegaly are variable and inconstant in the beginning. Ascites, because of a severe hyposerinemia, is frequent. The nutritional state is seldom impaired; the patient may be subfebrile. Hemorrhages, portal hypertension are rare. The blood formula is not characteristic. Hyperserinemia and hypocholesterolemia (including chiefly esterified cholesterol) are reliable laboratory data. Laparoscopy is of great clinical interest, perhaps equal to liver puncture, but without risks.

Franz J. Lust

RECHERCHES SUR L'ETAT FONCTIONNEL DES VOIES BILIARES ET DU PANCREAS AU COURS DE L'HEPATITE A VIRUS: Barnabe Laszlo. Acta gastroenterol. belg. 18:97 (Feb.), 1955.

The author studies the state of the biliary ducts and of the pancreas during the different stages of viral hepatitis. Biliary ducts are explored by the "timed duodenal intubation" following Varela Lopez et al modified by Gosset and Lambling. The state of the pancreas is studied by measurement of fecal lipids, of the fermentary power of the duodenal secretions (with the ether–proof of Kalk-Friedrich), and of prostigmin induced serum amylase. In the beginning of the disease, tonus is rather exaggerated; in its acme there is atony; during convalescence, hypertonic dyskinesia is again predominant. In some patients, inflammatory disease of the biliary apparatus appears, with fever, generally during the third or fourth week of convalescence. Deficiencies of the pancreatic functions (fermentary insufficiency) may take place too. The origin of the cholecystopancreatopathies following frequently chronic hepatitis or posthepatitis may lie–in a certain number of cases–in the functional disturbances, which take place during the acute phase of viral hepatitis. Laszlo has elaborated a pharmacodynamic procedure to verify the results of "timed intubation"; he associates his procedure with that of intubation. This combined method is recommended to differentiate functional spasm of the sphincter of Oddi from Vaterian organic stenosis.

FRANZ J. LUST

PORCELAIN GALLBLADDER WITH CARCINOMA OF THE GALLBLADDER: L. Lange. Fortschr. Roentgenstr. 82:411 (March), 1955.

Lange reports the case of a man, 51 years old, who had complaints for only one month. He had lost 7 kg. in weight. The roentgenological examination after oral Graham test failed to show a gallbladder. However, there was a round shadow of calcium deposit in the region of the gallbladder. At operation, a porcelain gallbladder was found. The specimen showed the same formation as seen on the roentgenogram. The pathological examination revealed a small scirrhus carcinoma of the gallbladder. It is apparently impossible to diagnose the carcinoma roentgenologically.

FRANZ J. LUST

GUIDING PRINCIPLES IN ATYPICAL EXERESIS OF THE LIVER: C. Couinaud. Presse Med. 21:417 (19 Mar.), 1955.

Atypical exeresis is an ablation of a part of the hepatic parenchyma rendered imperative by lesions: hemostasis is ensured by a barrier of imbricated stitches circumscribing the parenchyma to be removed. It is actually a blind procedure which runs the risk of harming vascular or biliary elements needed by the remaining parenchyma, a fact which explains most of the deaths said to be due to "hepatic deficiency" reported after these operations. Therefore regulated exeresis is superior because of the safeguard of the hemostasis and complete respect for the vasculobiliary elements needed for the remaining parenchyma.

However, atypical exereses have their value in certain circumstances: lesions on the edge of the liver, superficial lesions on the convex surface or on the lower surface, all those lesions whose topography and extent is such that regulated exeresis would entail too serious a sacrifice of the healthy part of the parenchyma. But they must comply with certain rules which the internal anatomy of the liver imposes. The sections must avoid the hilum region of the liver, the inferior vena cava, cutting the main right fissures which contain important suprahepatic veins, and in the main, never make deep incursions into the parenchyma but remain parallel to the peripheric edge of the liver. Furthermore, injury to important arterial or suprahepatic elements causes a change in the coloration of the distributing sector of these elements entailing the excision of the sector. The possible extent of these resections is studied from the topography.

GUY ALBOT

ACUTE AND CHRONIC CHOLECYSTITIS: Stephen W. Meagher and Alexander J. A. Campbell. New England J. Med. 252:615 (14 Apr.), 1955.

This is a study of 342 cases diagnosed preoperatively as cholecystitis during a two-year period; 99 were labeled acute, 230 as chronic. In the acute category 11 had no gallbladder disease, an error of 11.1 per cent; in the chronic division, no gallbladder pathology in 22 or 9.6 per cent of error. The condition found in the 11 erroneously diagnosed acute cases were: 4 acute appendicitis; 3 perforated peptic ulcer; 1 marginal ulcer; 1 pelvic abscess. Among the chronic errors were: one each of: regional ileitis, duodenal ulcer, fatty nutritional cirrhosis, duodenitis, mucus colitis; no diseased tissue found in 17. X-ray errors after Graham series was 4.9 per cent. Gallbladder disease was diagnosed in 33 cases by scout film, intravenous pyelograms, or previous laparotomy.

Common duct was explored in 44 chronic and 20 acute cases, with 43.2 per cent of the chronic and 30 per cent of the acute cases being positive.

Postoperative complications were listed as follows: Hypotension, Congestive cardiac, Acute pulmonary, Respiratory acidosis, Pulmonary abscess, Bile peritonitis, Pancreatitis, Subphrenic abscess, Subhepatic abscess, Cutaneous duodenal fistula, Wound sepsis, Incisional hematoma, Wound dehiscence and Phlebothrombosis.

In acute cases the mortality was 7.9 per cent; in those classified as emergency it was 13 per cent; but in acute cases treated by elective surgery it was only 3.9 per cent; and in the chronic cases the mortality was 1.9 per cent.

In 13 acute cases a perforated gallbladder was found, so that the total perforation percentage was 14.7 per cent. In 28 acute cases the gallbladder was palpable.

One or more attacks of acute pancreatitis occurred in 15 chronic cases and two of the acute gallbladder patients had acute pancreatitis. In only two of the pancreatitis patients were both cholelithiasis and choledocholithiasis discovered. One patient in the chronic classification had choledocholithiasis, pancreatitis, and a spontaneous cholecystoduodenal fistula. Twenty of the group had either duodenal ulcers or evidence of previous ulceration; three had gastric ulceration. Among the rarer findings were one case each of: remnant of the cystic duct containing gravel; dilated cystic duct remnant with common duct stone; spontaneous cholecystogastric fistula; spontaneous cholecystoduodenal fistula with stone in the common duct; diverticulum of the gallbladder; mucous polyp of the gallbladder; epidermoid carcinoma of the gallbladder; adenocarcinoma of the gallbladder associated with acute cholecystitis.

The author stresses the need for more conservatism. Surgery in acute cholecystitis increases the morbidity as well as the mortality. It is advisable to prepare the patient adequately. Alarm is unjustified with a palpable or perforated gallbladder, as the spillage will almost always be walled-off. Palpable, tender gallbladder is not a valid reason for immediate surgery. It is better to place the patient on a strict therapeutic regimen in preparation for later surgery. In summation the author states that the gallbladder should not be treated surgically without an adequate period of preparation.

REGINALD B. WEILER

DISEASES OF THE GALLBLADDER: THEIR NATURE AND CLASSIFICATION: Murray R. Abell. Canad. M.A.J. 72:565 (15 Apr.), 1955.

The etiological role of chemical irritants in the production of cholecystitis is considered of greater importance than that of bacteria, although the latter cannot be completely dismissed. The histological criteria for the various types of inflammation are discussed. Of interest is chronic lymphofollicular cholecystitis which may indicate that the patient is a typhoid or paratyphoid carrier, though this is not pathognomonic. Most clinical examples of acute cholecystitis actually represent acute exacerbations of a chronic or recurrent cholecystitis.

Benign neoplasms and neoplasm-like lesions of the gallbladder are uncommon. Hepatic, pancreatic, gastric, and intestinal choristomas are rare developmental abnormalities of interest only to the pathologist. Cases of carcinoma of the gallbladder and the extrahepatic bile ducts comprised 0.89 per cent of 12,838 autopsies performed at University Hospital (Ann Arbor, Michigan), 3.08 per cent of necropsies disclosing malignant neoplasms, and 5.09 per cent of all

necropsies with carcinomas. Carcinoma of the bile ducts was more frequent than that of the gallbladder. The histological features of the various neoplasms are discussed briefly and some of the more interesting types illustrated.

ARNOLD L. BERGER

CHOLOGRAFIN: R. Hastings-James and A. J. Glazebrook: Canad. M.A.J. 72:561 (15 Apr.), 1955.

Examination with chologrefin was helpful in 6 of 30 cases studied, supplying information not obtainable by oral methods of investigation. The test is recommended as an adjunct to oral methods, but it is not believed that at present it can displace the well-tried Graham test. There is doubt whether preliminary testing has any value except possibly from the medicolegal point of view. There were no cases of serious reactions. It is recommended that only three minutes be taken for the injection, rather than ten, and use 40 c.c. as a routine, except in very small patients. The first film is taken as soon as the injection is completed and the second at seven minutes; thereafter, each case must be treated individually. The time taken for the first opacification of the common bile duct varied from immediately after injection to 60 minutes. A pyelogram was seen in 14 of the 30 cases studied. The authors feel that the test's value lies in its simplicity and lack of special preparation needed by the patient, as well as independence on the absorptive powers of the alimentary tract. It gives some idea of liver function, but does not seem to parallel the usual laboratory tests. Its ability to show the common bile duct in the absence of the gallbladder forms the sole absolute indication and may be of the greatest help in patients after cholecystectomy. Another indication would be failure to visualize the gallbladder after the Graham test.

ARNOLD L. BERGER

CONGENITAL ATRESIA OF THE BILE DUCTS: Rodney Maingot: Brit. M. J. 4924:1256 (21 May), 1955.

According to the author, 38 cases of congenital atresia of the extrahepatic bile ducts have been successfully treated by surgery. Rodney Maingot records a successful cholecystojejunostomy combined with jejunojejunostomy for atresia of the common bile duct. The preoperative treatment and differential diagnosis is discussed in detail. He concludes that a newborn child with jaundice should be subjected to exploratory operation shortly after the diagnosis of obstructive jaundice is made. A search must then be made for any evidences of extrahepatic biliary passages which might be used to establish a free flow of bile into the intestinal tract. Fully 20 per cent of the cases of atresia of the bile duct can be cured by operation. In the case reported, the child operated upon was less than two months of age and has been followed for more than three years. When last seen "he looked the picture of health and was developing normally".

IRVIN DEUTSCH

THE EFFECT OF VITAMIN B_{12} AND FOLIC ACID IN THE TREATMENT OF VIRAL HEPATITIS: Robert E. Campbell and Francis W. Pruitt. International Med. Dig. 66:272 (May), 1955.

Vitamin B_{12} and folic acid play a role in nucleic acid synthesis as well as exert a protective action in liver damage. Therefore, the authors administered 30 micrograms of Vitamin B_{12} intramuscularly daily and 5 mg. of folic acid orally three times a day for ten days during the initial stage of virus hepatitis. All patients were carefully matched with controls. Those receiving Vitamin B_{12} and folic acid showed a return of the increased serum bilirubin to normal within 11 weeks while the controls required 18 weeks for reaching the same stage of recovery. Similarly the delay of BSP elimination was overcome in a much shorter period of time by the treated group. It is the opinion of the authors that B_{12} and folic acid therapy combined is beneficial for hepatic repair in virus hepatitis.

H. B. EISENSTADT

PATHOLOGY AND LABORATORY RESEARCH

TREATMENT OF CLONORCHIASIS WITH CHLOROQUINE AND METHISCHOL: Paul S. Crane et al. Trans. Roy Soc. Trop. Med. & Hygiene 49:68-70 (Jan.), 1955.

Thirty-four patients with *C. sinensis* infections were treated with chloroquine and methischol. The stools of 12 were free of clonorchis eggs 1 months after treatment was completed. This may be of importance both because of the heavy infections in these Korean patients (where this study was done) and because the usual treatment with gentian violet is dependably undependable.

KERMIT G. DWORK

EFFECTS OF ANTICHOLINERGIC DRUGS ON PEPSIN PRODUCTION AND UROPEPSINOGEN EXCRETION: Harold M. Silver, Helio Pucci and Thomas P. Almy. New England J. Med. 252:520 (31 Mar.), 1955.

This study was undertaken to observe the effects of anticholinergic agents on gastric secretion of pepsin. Because experiments exhibited significant pepsin depression, it was decided to explore uropepsinogen excretion as a measure of testing such activity. Gastric cells responsible for secreting pepsin simultaneously pour pepsinogen into the circulation. Under basal conditions, the ratio between gastric and urinary pepsinogen has been found to be 1:99.

In ten subjects intravenous administration of Methantheline (Banthine) resulted in a prompt fall of pepsin values by some 21 per cent but the relative concentration of pepsin was practically unaltered. Oral exhibitions of propantheline (Pro-Banthine) reduced urinary uropepsinogen excretion to about 78 per cent of basal values.

The use of uropepsinogen as a measure of the effect of antisecretory drugs has a number of advantages. It reflects the significance of emotions and stresses on the individual's gastric functions. A much more realistic outlook is thus obtainable under living conditions rather than the picture represented by controlled laboratory studies. In as much as the emotional reactivity contributes markedly to ulcer formation and ulcer cure such information as is obtained under usual environmental conditions is a better index of the importance of antisecretory regimes than that found under laboratory control. Further, this measure of uropepsinogen excretion affords a method of study over periods of weeks rather than only of hours. It is not to be discounted that the procedure requires only a nocturnal collection of urine which certainly is less upsetting psychologically and less time consuming than gastric intubation.

REGINALD B. WEILER

TREATMENT OF ENTEROBIUS VERMICULARIS INFECTIONS WITH PIPERAZINE: H. W. Brown and K. F. Chan. Am. J. Trop. Med. & Hygiene 4:321-325 (Mar.), 1955.

Piperazine citrate has previously been shown to be effective in treating pinworm disease. This carefully conducted study with 120 patients is a further effort to determine optimum treatment schedules. The authors find that treatment with piperazine is most effective against human pinworm infection when 14 consecutive days of treatment are given at the usual dose levels. This is in contrast to previously recommended schedules of 1 week treatment followed by 1 week rest followed by 1 week treatment.

KERMIT G. DWORK

THE DIMINUTIVE ENDAMEBA HISTOLYTICA: A REVIEW OF THE LITERATURE OF SMALL RACE AMEBAE WITH ADDITIONAL NOTES BASED ON A RECENT SURVEY: Kermit G. Dwork, A. X. Rossien and Deborah Friedman. Mississippi Valley M. J. 4:113 (July) 1955.

This is a technical paper on the size of *Endameba histolytica* cysts and trophozoites and their clinical significance. It is pointed out that the size of the parasites does not preclude the production of symptoms and that all sizes should be considered pathological and treated accordingly. One case of small race infection had an eight month cure after a standard course of carbarsone therapy.

ABE ALPER

BOOK REVIEWS FOR GASTROENTEROLOGISTS

A TEXTBOOK OF MEDICINE: Russell L. Cecil, M.D., Sc.D., Professor of Clinical Medicine Emeritus, Cornell University, New York, N. Y. and Robert F. Loeb, M.D., Sc.D., D. Hon. Causa, LL.D., Bard Professor of Medicine, Columbia University, New York, N. Y. Associate Editors: Alexander B. Gutman, M.D., Ph.D., Professor of Medicine, Columbia University, New York, N. Y.; Walsh McDermott, M.D., Livingston Farrand Professor of Public Health and Preventive Medicine, Cornell University, New York, N. Y. and Harold G. Wolff, M.D., Professor of Medicine (Neurology), Cornell University, New York, N. Y. Ninth Edition. 1,786 pages, illustrated. W. B. Saunders Co., Philadelphia, Pa., 1955. Price $15.00.

With its many contributors, that this voluminous text has reached its ninth edition, is no small compliment. It is a veritable storehouse of information on medicine as a whole. Medical students, general practioners and specialists in all branches of medicine will find this well written illustrated volume a welcome addition to their library.

The editors, contributors and especially the publisher, deserve great credit in making this book the outstanding text in the field of medicine.

ANNUAL REVIEW OF MEDICINE: David A. Rytand, M.D. and J. A. Anderson, M.D. 459 pages. Annual Reviews, Inc., Stanford, Calif, Vol. 6, 1955. Price $7.00.

This sixth volume, as well as the other volumes in these series, bring to the physician a comprehensive review of medicine as a whole. The co-authors of these volumes are specialists in their field and the extensive literature cited at the end of each special subject adds to the value of this volume.

The introduction by Bloomfield is commendable and should be read, as it describes the beginning of medical literature abroad and in this country.

Although one may not specialize in infectious diseases (viruses), nonetheless the reviewer recommends that the physician read the chapter. He will be well paid for the time spent; so also with diseases of the gastrointestinal tract (liver). A very important point is brought to the attention of the practitioner regarding the length of bed rest in acute viral hepatitis. A recent study of patients with this type of hepatitis in United States troops in Germany and Korea, brought about a change in the practice of keeping patients in bed for six to eight weeks. The decision arrived at was that these patients should be kept in bed in the early stages and as soon as the patient begins to feel well, regardless of the jaundice, confinement to bed is not necessary. Further proof is obtained by determining the serum bilirubin, if it is 1.5 mg. per cent or lower, for one week and bromsulfalein retention, less than 6 per cent after 45 minutes, for a similar period of time, then, the patient should be discharged from the hospital. In civilian practice, this may not work out so readily, as in many patients the bromsulfalein retention may remain at a higher percentage, even though the patient may feel well. In these cases, it is advisable to proceed with caution to prevent recurrence or to develop a chronic state.

The reviewer enjoyed reading the entire volume and recommends it highly to all physicians as well as medical students.

TRANSACTIONS OF THE FIFTH MEETING OF THE INTERNATIONAL SOCIETY OF GEOGRAPHICAL PATHOLOGY, Washington, D. C., 6-11 September 1954. 950 pages, illustrated. S. Karger, A.G., Basel, Switzerland, 1955. Price SFr. 67.60.

A very interesting volume of transactions dealing with cancer of the various organs in the human race as found in the several nationalities. The participants are of high caliber, who have devoted their best years in trying to solve this great scourge.

These transactions are recommended to be read and reread by the physician, provided he finds time in his busy practice.

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INDEX

TO

VOLUME 25

JANUARY—JUNE 1956

PAGES 1—626

SUBJECT INDEX

A

Page

Abdominal Pain, Nausea and Vomiting, Without–, Due to Giardiasis 131
Abdominal Manifestations of Sickle Cell Anemia 11
Abdominoperineal Resection, Complications of 463
Abstracts:
  Esophagus 599
  Gastrointestinal Tract 595
  Intestines 603
  Liver and Biliary Tract 605
  Pathology and Laboratory Research 609
  Stomach 601
Achalasia, Cricopharyngeal 45
Acute and Chronic Relapsing Pancreatitis 234
Adrenal Influences Upon the Gastrointestinal Tract 532
Amebiasis, The Pathogenesis and Therapy of Human 315
Anemia, Abdominal Manifestations of Sickle Cell 11
Anesthesia:
  Improved– for Gastroscopy (Editorial) 177
  Newer Trends in Caudal 555
Aneurysms, Intraabdominal Symptoms Due to 333
Annual Review of Medicine, 1955 (Book Review) 610
Anorectal Complications of Chronic Ulcerative Colitis and Regional Enteritis 472
Anticholinergic Medication, Cardiospasm: Favorable Results With 454
Antral and Pyloric Musculature, Hypertrophic– in the Adult 486
Association of Liver Disease with Ulcerative Colitis, The 172

B

Bacteria, The Role of– in the Gastrointestinal Tract with Changing Concepts of Intestinal Function 22
Barium Suspended in Hydrogen Peroxide in the Radiological Diagnosis of the Stomach and Duodenum 415
Benign Duodenal Tumors: Three Case Reports 355
Biopsy:
  –of the Liver, The Value of 253
  Status of Liver–, The 33
Bowel, X-ray Lesions of the Small 575

C

Carcinoma:
  –of the Descending Colon to the Rectosigmoid 571
  –of the Pancreas 59
  –of the Sigmoid Colon Discovered During Examination for Acute Intussusception of the Sigmoid 591
  –of the Stomach, Lymphatic Leukemia Complicated by 116
  –of the Stomach, Surviving After Surgery More Than Twelve and Eight Years Respectively, Two Cases 550
Cardiospasm: Favorable Results with Anticholinergic Medication 454
Caudal Anesthesia, Newer Trends in 555
Cirrhosis of the Liver, Splenic Venography in Portal 363
Clinical Disorders of Hydration and Acid-Base Equilibrium (Book Review) 502
Clinical Significance of Acute Porphyria, The 266

Colitis:
Anorectal Complications of Chronic Ulcerative– and Regional Enteritis 472
Association of Liver Disease with Ulcerative–, The 172
Colon:
Carcinoma of the Descending– to the Rectosigmoid 571
Carcinoma of the Sigmoid– Discovered During Examination for Acute Intussusception of the Sigmoid 591
Irritable–, A Bad Term 176
Colonic Diverticulitis 584
Complications of Abdominoperineal Resection 463
Cricopharyngeal Achalasia 45

D

Diaphragmatic (Hiatal) Hernia 38
Digestive Disorders, Experience With Serpasil on 439
Digestive System, Disorders of the– : Brief Review of Major Existing Problems 525
Dihydroxy Aluminum Aminoacetate, The Efficacy of– in the Medical Cure of Peptic Ulceration 74
Disorders of the Digestive System: Brief Review of Major Existing Problems 525
Diverticulitis, Colonic 584
Diverticulosis of the Gallbladder 154
Duodenal Tumors, Benign– Three Case Reports 355
Duodenal Ulcer, The Importance of Proper Acid Neutralization in the Management of Gastric and 66
Duodenum, Barium Suspended in Hydrogen Peroxide in the Radiological Diagnosis of the Stomach and 415
Dysphagia, Functional Causes of 51

E

Effects of a Low Fat Diet on the Incidence of Gallbladder Disease, The 158
Effects of Reserpine on Gastric Secretion 430
Efficacy of Dihydroxy Aluminum Aminoacetate in the Medical Cure of Peptic Ulceration, The 74
Emphysematous Gastritis 125
Enteritis, Anorectal Complications of Chronic Ulcerative Colitis and Regional 472
Esophagoscopy, The Gastroscopist's Adaptation to 272
Experience with Serpasil on Digestive Disorders 439
Experiences with Transabdominal Supradiaphragmatic Vagotomy 419

F

Fluoroscopy in Diagnostic Roentgenology (Book Review) 501
Functional Causes of Dysphagia 51
Functional Hypoglycemia 225

G

Gallbladder:
Diverticulosis of the 154
Effects of a Low Fat Diet on the Incidence of– Disease, The 158
Gastric and Duodenal Ulcer, The Importance of Proper Acid Neutralization in the Management of 66
Gastric Secretion, Effects of Reserpine on 430
Gastritis, Emphysematous 125
Gastroenterological Diagnostic Procedures, Special 137

Gastroesophageal Regurgitation, Heartburn During Pregnancy, Hiatal Hernia and (Editorial) 498
Gastrointestinal:
Adrenal Influences Upon the– Tract 532
Phrenic Nerves and– Mechanisms. Left Phrenic Crush and Vagotomy 545
Role of Bacteria in the– Tract with Changing Concepts of Intestinal Function, The 22
Gastroscopist's Adaptation to Esophagoscopy, The 272
Gastroscopy, Improved Anesthesia for (Editorial) 177
Giardiasis, Nausea and Vomiting, Without Abdominal Pain, Due to 131
Gluten Sensitivity–Sprue? 562
Granulomatous Disease, Nonspecific– of the Rectum Following Regional Ileitis 380

H

Heartburn During Pregnancy, Hiatal Hernia and Gastroesophageal Regurgitation (Editorial) 498
Hemorrhage, Pathologic Anatomy of Massive– in Peptic Ulcer 109
Hernia:
Diaphragmatic (Hiatal) 38
Heartburn During Pregnancy, Hiatal– and Gastroesophageal Regurgitation (Editorial) 498
Hydrogen Peroxide, Barium Suspended in– in the Radiological Diagnosis of the Stomach and Duodenum 415
Hypertrophic Antral and Pyloric Musculature in the Adult 486
Hypoglycemia, Functional 225

I

Ileitis, Nonspecific Granulomatous Disease of the Rectum Following Regional 380
Importance of Proper Acid Neutralization in the Management of Gastric and Duodenal Ulcer, The 66
Improved Anesthesia for Gastroscopy (Editorial) 177
Influence of Sex and Age on Uropepsin Excretion, The 346
Increased Uropepsin Excretion During Testosterone Administration 341
In Memoriam:
Upham, Roy 177, 278
Webb, Leslie R. 500
Weiss, Adolf A. 500
Intestinal Function, The Role of Bacteria in the Gastrointestinal Tract with Changing Concepts of 22
Intraabdominal Symptoms Due to Aneurysms 333
Ion Exchange and Absorption Agents in Medicine, The Concept of Intestinal Bionomics (Book Review) 502
Irritable Colon– , A Bad Term (Editorial) 176
Intussusception, Carcinoma of the Sigmoid Colon Discovered During Examination for Acute– of the Sigmoid 591

J

Jaundice:
Protracted 441
Some Perplexities in the Problem of 164

L

Les Gastrites (Book Review) 501
Lesions, X-ray– of the Small Bowel 575
Leukemia, Lymphatic– Complicated by Carcinoma of the Stomach 116

Liver:
—Biopsy, The Status of 33
—Disease with Ulcerative Colitis, The Association of 172
Splenic Venography in Portal Cirrhosis of the 363
Value of Biopsy of the—, The 253
Low Fat Diet, The Effects of a— on the Incidence of Gallbladder Disease 158
Lymphatic Leukemia Complicated by Carcinoma of the Stomach 116

N

Nausea and Vomiting, Without Abdominal Pain, Due to Giardiasis 131
Newer Trends in Caudal Anesthesia 555
News Notes 84, 179, 388, 500, 594
1954-55 Year Book of Endocrinology (Book Review) 502
1955 Medical Progress—A Review of Medical Advances During 1954 (Book Review) 501
Nonspecific Granulomatous Disease of the Rectum Following Regional Ileitis 380

P

Pancreas, Carcinoma of the 59
Pancreatitis, Acute and Chronic Relapsing 234
Panel Discussion on Peptic Ulcer 205
Pathogenesis and Therapy of Human Amebiasis, The 315
Pathologic Anatomy of Massive Hemorrhage in Peptic Ulcer 109
Peptic Ulcer:
Panel Discussion on 205
Pathologic Anatomy of Massive Hemorrhage in 109
Peptic Ulceration, The Efficacy of Dihydroxy Aluminum Aminoacetate in the Medical Cure of 74
Phrenic Crush, Phrenic Nerves and Gastrointestinal Mechanisms. Left— and Vagotomy 545
Phrenic Nerves and Gastrointestinal Mechanisms. Left Phrenic Crush and Vagotomy 545
Porphyria, The Clinical Significance of Acute 266
Portal Cirrhosis, Splenic Venography in— of the Liver 363
Portal Decompression, Present Status of— for Portal Hypertension 148
Portal Hypertension, Present Status of Portal Decompression for 148
Pregnancy, Heartburn During—, Hiatal Hernia and Gastroesophageal Regurgitation (Editorial) 498
Present Status of Portal Decompression for Portal Hypertension 148
President's Message 83, 178, 277, 387, 499, 593
Prolonged and Perplexing Fevers (Book Review) 501
Protracted Jaundice 441
Pyloric Musculature, Hypertrophic Antral and— in the Adult 486

R

Radiological Diagnosis, Barium Suspended in Hydrogen Peroxide in the— of the Stomach and Duodenum 415
Rectosigmoid, Carcinoma of the Descending Colon to the 571
Rectum, Nonspecific Granulomatous Disease of the— Following Regional Ileitis 380
Regional Ileitis, Nonspecific Granulomatous Disease of the Rectum Following 380
Regurgitation, Heartburn During Pregnancy, Hiatal Hernia and Gastroesophageal (Editorial) 498
Resection, Complications of Abdominoperineal 463
Reserpine, Effects of— on Gastric Secretion 430
Role of Algae and Plankton in Medicine, The (Book Review) 502
Role of Bacteria in the Gastrointestinal Tract with Changing Concepts of Intestinal Function, The 22

S

Secretion, Effects of Reserpine on Gastric 430
Serpasil, Experience with— on Digestive Disorders 439
Sickle Cell Anemia, Abdominal Manifestations of 11
Sigmoid, Carcinoma of the— Colon Discovered During Examination for Acute Intussusception of the Sigmoid 591
Some perplexities in the Problem of Jaundice 164
Special Gastroenterological Diagnostic Procedures 137
Splenic Venography in Portal Cirrhosis of the Liver 363
Sprue?, Gluten Sensitivity 562
Status of Liver Biopsy, The 33
Stomach:
Barium Suspended in Hydrogen Peroxide in the Radiological Diagnosis of the— and Duodenum 415
Two Cases of Carcinoma of the— Surviving After Surgery More Than Twelve and Eight Years Respectively 550
Lymphatic Leukemia Complicated by Carcinoma of the 116

T

Testosterone, Increased Uropepsin Excretion During— Administration 341
Textbook of Medicine (Book Review) 610
Transabdominal Supradiaphragmatic Vagotomy, Experiences with 419
Transactions of the Fifth Meeting of the International Society of Geographical Pathology 610
Tumors, Benign Duodenal— : Three Case Reports 355

U

Ulcer:
Importance of Proper Acid Neutralization in the Management of Gastric and Duodenal—, The 66
Panel Discussion on Peptic 205
Pathologic Anatomy of Massive Hemorrhage in Peptic 109
Ulceration, The Efficacy of Dihydroxy Aluminum Aminoacetate in the Medical Cure of Peptic 74
Ulcerative Colitis:
Anorectal Complications of Chronic— and Regional Enteritis 472
Association of Liver Disease with—, The 172
Uropepsin:
Increased— Excretion During Testosterone Administration 341
Influence of Sex and Age on— Excretion, The 346

V

Vagotomy:
Experiences with Transabdominal Supradiaphragmatic 419
Phrenic Nerves and Gastrointestinal Mechanisms. Left Phrenic Crush and 545
Value of Biopsy of the Liver, The 253
Venography, Splenic— in Portal Cirrhosis of the Liver 363
Verhandlungen der Deutschen Gesellschaft für Verdauungs und Stoffwechselkrankheiten (Book Review) 581
Vomiting, Nausea and—, Without Abdominal Pain, Due to Giardiasis 131

X

X-ray Atlas and Manual of Esophagus, Stomach and Duodenum (Book Review) 191
X-ray Lesions of the Small Bowel 575

INDEX TO AUTHORS

A-B

Anderson, J. A. 610
Balfour, Donald C. 341
Barborka, Clifford J. 205
Bassler, Anthony 176
Beasley, L. K. 575
Bohrod, Milton G. 109
Bolt, Robert J. 205
Brenner, Abraham J. 116
Bridgewater, Anna B. 346

C-D

Canahuati, Shibli 441
Carroll, Walter W. 205
Cecil, Russell L. 610
Chaudhury, C. Roy 363
Child, Charles G., III 148
Christian, Edward R. 253
Coleman, John M. 419
Cornet, A. 501
Creek, D. W. 225
Dailey, U. G. 545
Dalessandro, William 441
DeLorimier, A. A. 486
Deutschberger, Otto 501

E-F

Eichhorn, Ralph 125
Epstein, Bernard S. 116
Eusterman, George B. 525
Farfel, Bernard 125
Feigenbaum, Harry A. 591
Fishbein, Morris 501
Frye, William W. 315

G-H

Gianturco, C. 415
Gordan, Gilbert S. 502
Granet, Emil 472
Gray, Seymour J. 532
Hall, D. P. 154
Heineken, Theodore S. 584
Hufford, A. Ray 272

I-J

Jefferson, N. C. 545

K-L

Kanin, Harry J. 172
Kaplan, Murrel H. 234
Karger, S. 610
Keefer, Chester S. 501
Konar, N. R. 363
Krakauer, Lewis J. 532
Leard, Samuel E. 501
Lee, Jennie 137
Levin, Irving A. 463
Levin, Jack J. 172
Levin, Myron J. 555
Lewis, R. Burns 205
Lindert, M. C. F. 172
Litwins, Joseph 562
Loeb, Robert F. 610

M-N

Martin, Gustav J. 502
Matzner, Milton J. 177, 454
McBurney, Robert 59
McMahon, John M. 51
Miller, G. A. 415
Monat, Henry A. 439
Morrison, Lester M. 158
Moutier, F. 501
Necheles, H. 346, 545
Nieda, I. 486
Nix, James T. 45

O-P

Ogden, W. W. 463
Posey, E. L., Jr. 38
Puestow, Karver L. 22

Q-R

Ramsey, Colin G. 532
Redeker, Allan G. 266
Reifenstein, Robert W. 532
Rice, Marion L. 74
Rider, J. Alfred 137
Riese, Jacob A. 66
Rose, Raymond F. 555
Rosi, Peter A. 571
Rossett, N. E. 33
Rossman, Melvin E. 430
Rudner, Henry G., Jr. 11
Rudner, Henry G., Sr. 11
Rukstinat, George J. 333
Rytand, David A. 61

S-T

Sadove, Max S. 555
Sanders, L. C. 59
Schwartz, Sheldon 355
Schwimmer, David 502
Schwimmer, Morton 502
Scimeca, Michael 550
Serwer, Jesse J. 131
Sheinfeld, William I. 355
Sorter, H. 346
Steigmann, Frederick 441
Stephenson, S. L., Jr. 38
Strub, Irving H. 419
Tesler, James 550
Texter, E. Clinton, Jr. 205
Torrey, Francis A. 555

U-V

van der Reis, Leo 137
Vaughn, Arkell M. 419
Vogel, Frederick 380
Vorhaus, Louis J., II 164

W-X-Y-Z

Walker, L. 545
Weingarten, Michael 131
Weiss, Samuel 498
Welt, Louis G. 502
Windwer, Charles 454
Wolf, Julius 430

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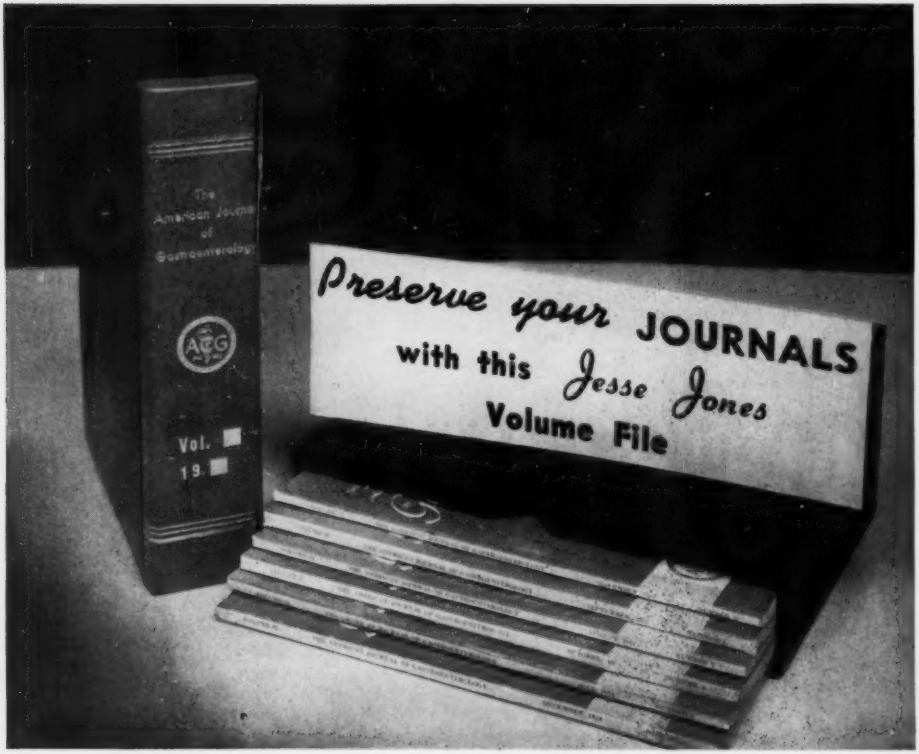

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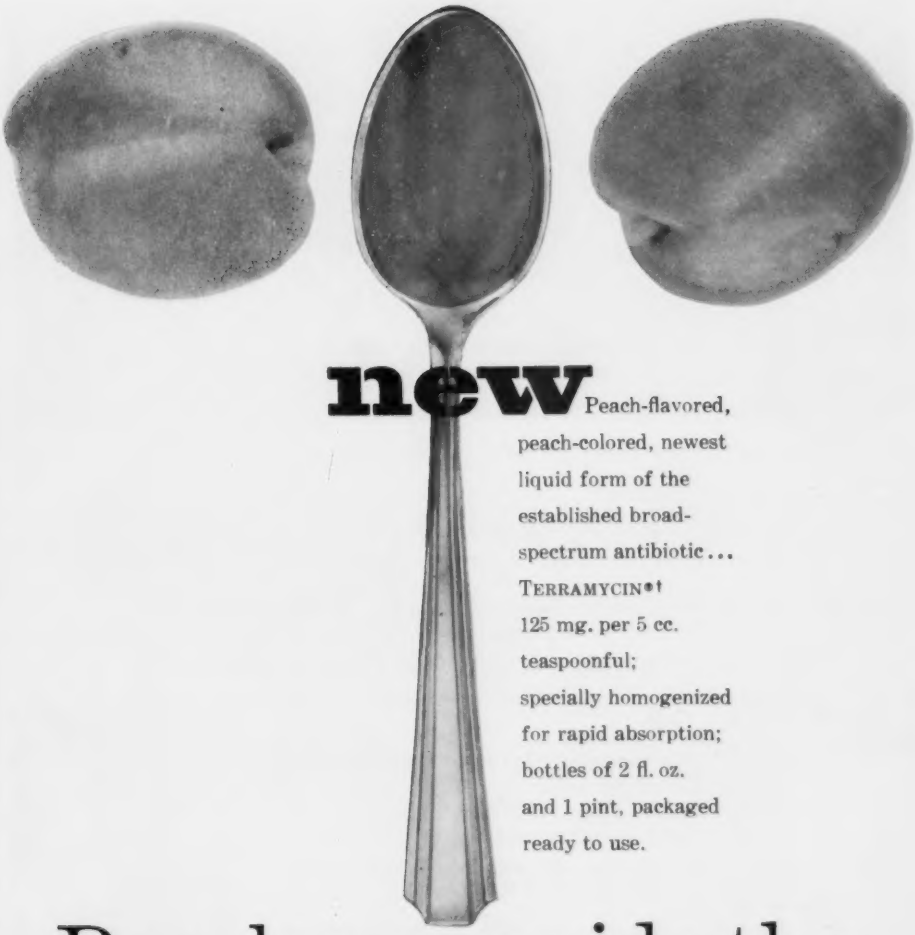

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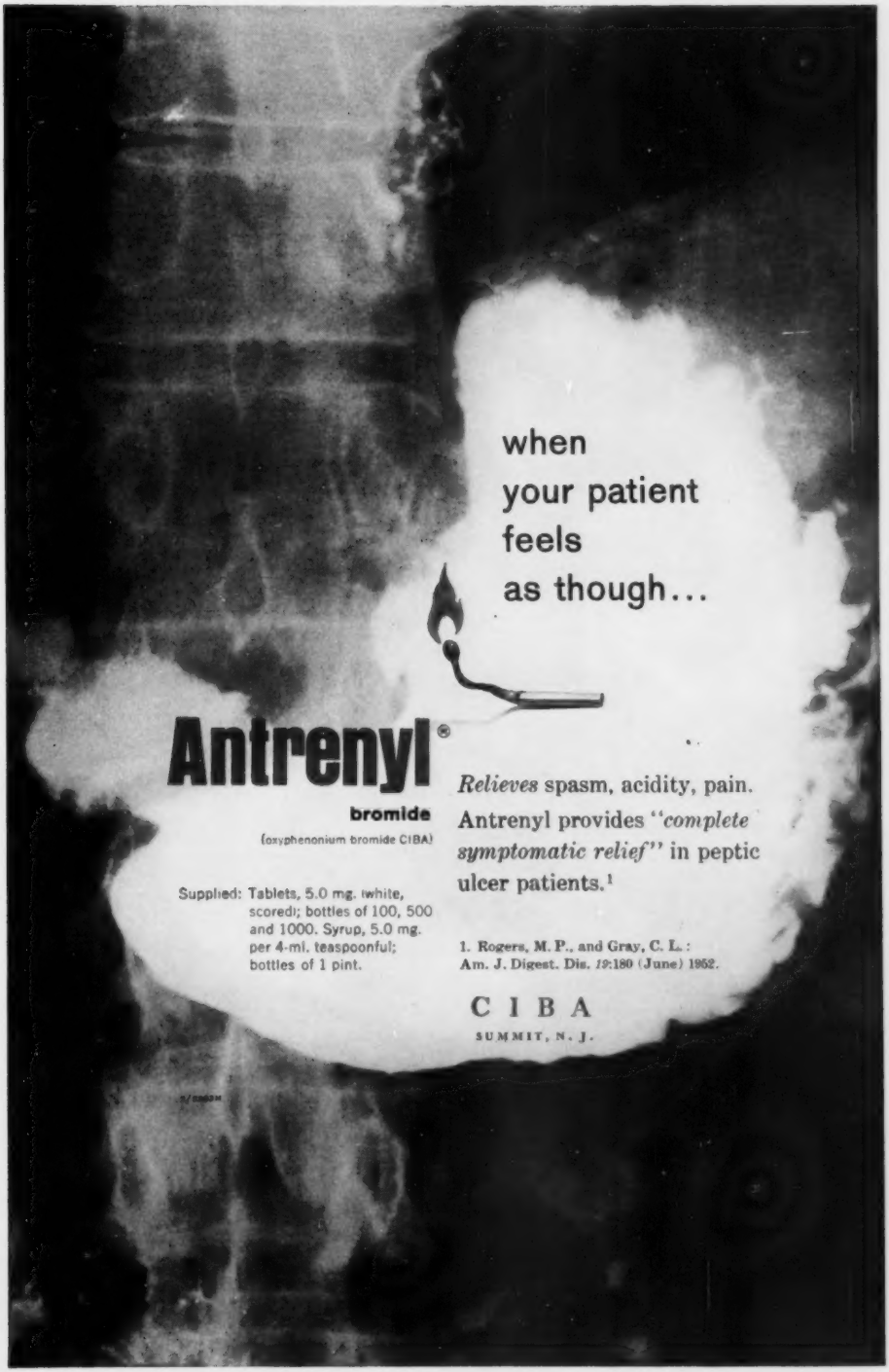
when
your patient
feels
as though...
Antrenyl®
bromide
(oxyphenonium bromide CIBA)
Supplied: Tablets, 5.0 mg. (white, scored); bottles of 100, 500 and 1000. Syrup, 5.0 mg. per 4-ml. teaspoonful; bottles of 1 pint.
Relieves spasm, acidity, pain. Antrenyl provides "*complete symptomatic relief*" in peptic ulcer patients.[1]
1. Rogers, M. P., and Gray, C. L.: Am. J. Digest. Dis. 19:180 (June) 1952.
CIBA
SUMMIT, N. J.

for the "Sippy-diet" patient

a welcome *(and often necessary)* change from "milk-and-cream"

MULL-SOY® Powdered

Pioneer soy alternative to milk . . . reported to be "noticeably more soothing to the upper gastrointestinal tract and seemingly easier to digest."[1] Comparable to milk in buffering[2] and nutritional[3] qualities. Contains no cholesterol . . . and costs the patient *much* less than milk-and-cream. Easy to prepare—4 level tablespoonfuls to 8 oz. water. In 1-lb. tins at all drug outlets.

1. Balfour, D. C., Jr.: Am. J. Gastroenterol. 22:181, 1954. 2. Burke, J. O., et al.: Internat. Rec. Med. & Gen. Practice Clin. 167:587, 1954. 3. Sternberg, S. D., and Greenblatt, I. J.: Ann. Allergy 9:190, 1951.

Are you wondering how MULL-SOY Powdered tastes? Return this coupon for professional trial samples and see for yourself how *pleasant* it can be for your milk-weary or milk-intolerant ulcer patients.

THE BORDEN COMPANY
Prescription Products Division, Dept. 204
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Please send to me, without charge, four 4-oz. tins of MULL-SOY Powdered.

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pronounced
MUSCLE-RELAXING ACTION

Equanil*

MEPROBAMATE (2-methyl-2-*n*-propyl-1,3-propanediol dicarbamate)

LICENSED UNDER U.S. PATENT NO. 2,724,720

For significant relief in myositis, osteoarthritis, backstrain, and related conditions marked by:

- ***Muscle spasm***
- ***Stiffness and tenderness***
- ***Restriction of motion***
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As a superior muscle-relaxant, EQUANIL offers predictable action and full effectiveness on oral administration. It does not disturb autonomic function and is relatively free from gastric and other significant side-effects. Its anti-anxiety property provides important correlative value.

Usual dosage: 1 tablet t.i.d. The dose may be adjusted either up or down, according to the clinical response of the patient.
Supplied: Tablets, 400 mg., bottles of 50.

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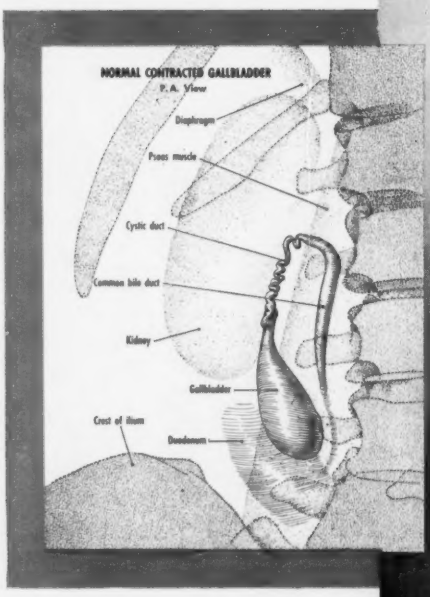
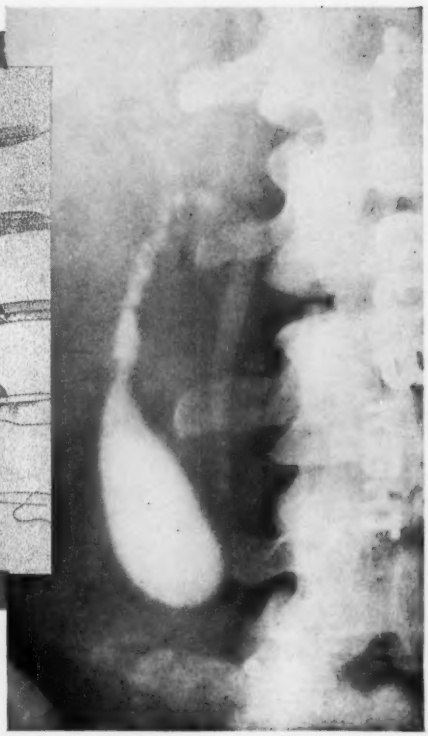
anti-anxiety factor
with muscle-relaxing action
. . . relieves tension

*TRADEMARK





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1. **Excellent cholecystograms are readily obtainable.**
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3. **In a fairly large percentage of cases, the cystic and the common ducts are quite definitely outlined, and occasionally even the hepatic duct."**

Buckstein, Jacob: The Digestive Tract in Roentgenology. Philadelphia, J. B. Lippincott Co., 2nd ed., 1953, vol. 2, p. 1003.

DOSAGE:

The average adult dose of Telepaque is 3 Gm. (6 tablets). In persons of thin or medium build, weighing less than 150 lb., 2 Gm. (4 tablets) may be sufficient.

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Tablets of 0.5 Gm. in envelopes of 6 tablets, boxes of 5 and 25 envelopes, and bottles of 500.

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For abnormal bowel physiology use

L. A.® Formula

It is important, when inducing normal bowel function, to supply a non-irritating bulk to the colon, especially in those cases in which it has been necessary to eliminate from the diet the high roughage foods containing irritating bulk (lignin and cellulose).

It has been shown[1] that the colon resumes a more normal peristaltic pattern[2] when it is supplied with a stool of medium soft consistency of sufficient bulk[3], especially if the indigestible portion of that bulk consists primarily of hemicellulose[4].

L. A. FORMULA is a vegetable concentrate of naturally occurring hemicelluloses. It is derived from blond psyllium seed by our special Ultra-Pulverization Process and simultaneously dispersed in lactose and dextrose. It provides just the moist, smooth, effective[5] bulk so essential to normal peristalsis.

Furthermore. **L. A. FORMULA** is undetectable in fruit juice and milk, pleasant tasting in water, and available in 7 and 14 ounce containers at significantly lower cost-to-patient prices. That's why we say **"L. A. FORMULA . . . to normalize."**

...to normalize

1. Dolkart, R. E., Dentler, M., & Barrow, L. L., Illinois M. J., 90:286, 1946
2. Adler, H. F., Atkinson, A. J., & Ivy, A. C., Am. J. Digest. Dis., 8:197, 1941
3. Wozasek, O., & Steigman, F., Am. J. Digest. Dis., 9:423, 1942
4. Williams, R. D. & Olmsted, W. H., Ann. Int. Med., 10:717, 1936
5. Cass, L. J. & Wolf, L. P., Gastroenterology, 20:149, 1952

Formula: 50% plantago ovata coating dispersed in lactose and dextrose.

Made by BURTON, PARSONS & COMPANY *Since 1932*

Originators of Fine Hydrophilic Colloids

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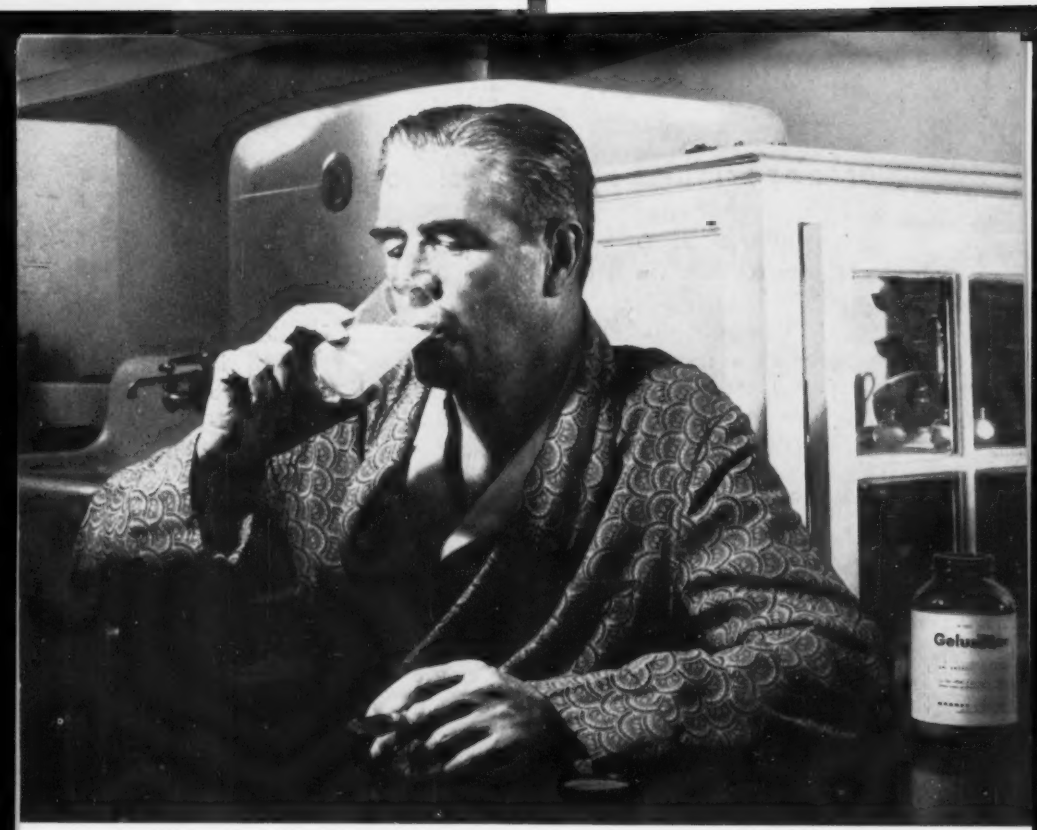

to pass "the acid test" day and night

Gastric hyperacidity checkmated: Acute or chronic gastric hyperacidity can now be held in check both day and night, with Gelusil and the new formulation, Gelusil-Lac.

Sustained daytime antacid protection: The sustained action of magnesium trisilicate and specially prepared aluminum hydroxide gel restores and maintains the gastric pH within the normal range, without overneutralizing or alkalizing. Gelusil thus avoids the twin dangers of acid rebound and systemic alkalosis.

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Nonconstipating: Gelusil's aluminum hydroxide component is of a low order of chemical reactivity, hence the formation of astringent — and constipating — aluminum chloride is minimal.

Dosage: 2 Gelusil tablets or 2 teaspoonfuls of Gelusil liquid two hours after eating or when symptoms are pronounced. Each tablet or teaspoonful provides: 7½ gr. magnesium trisilicate and 4 gr. aluminum hydroxide gel. Gelusil-Lac: at bedtime, one heaping tablespoonful stirred rapidly into one-half glass (4 fl. oz.) of cool water. (Provides equivalent of 4 Gelusil tablets.)

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